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ARCHIVES OF SURGERY

VOLUME 29 SEPTEMBER 1934 NUMBER 3

REMOVAL OF CEREBELLOPONTILE (ACOUSTIC) TUMORS THROUGH A UNILATERAL APPROACH

WALTER E. DANDY, M.D.
BALTIMORE

For the attack on the well recognized encapsulated tumors of the cerebellopontile angle (erroneously, I think, called acoustic tumors) the bilateral cerebellar approach has been adopted by all neurosurgeons. I know of no exception to this rule. The purpose of this communication is to present a radical departure from this standardized approach, namely, to offer in its stead, a unilateral exposure, essentially similar to that now used when the fifth, eighth and ninth nerves are divided for various symptoms referable to these nerves.

Originally a unilateral approach was proposed by Krause; it was used by others and subsequently given up because it was entirely inadequate. A pertinent query is, therefore, Why again propose a seemingly similar approach which has been proved to have disastrous consequences? The answer is that new developments, particularly methods of space reduction, then not known or not properly appreciated, now offer all of the advantages obtained by the more extensive exposure. It is well known to those who have had much experience with these tumors that the patient's resources may be so severely taxed by the bilateral approach alone, particularly with the bloody midline, that the additional attack on the tumor at the same operation may be inadvisable. For many years surgeons, at least those in this country, have used the tremendous exposure provided by the so-called cross-bow incision of Cushing. Perhaps a decade ago, I gave this up for the more simple, less bloody and less arduous transverse incision, which is curved downward at the mastoid processes. This provides the same exposure and makes the approach to the angle easier, because the big nuchal muscles fall away from, rather than toward, the line of vision. Moreover, the cerebrospinal fistulas that developed all too frequently in the vertical part of the cross-bow incision, with many disastrous sequelae, were automatically avoided. The transverse incision which I [1] employed was much like that

1. Dandy, W. E.: An Operation for the Total Removal of Cerebellopontile (Acoustic) Tumors, Surg. Gynec. & Obst. **41**:129, 1925. Cerebellopontine (Acoustic) Tumors, in Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1933, vol. 12, chap. 1, p. 534.

proposed by Cotterill [2] in 1899, but it was modified by enlarging the cutaneous incision and bony defect upward and outward on the side of the tumor. Gradually the conclusion was forced on me that, after the other items in space compensation had been put into effect, the bilateral bony defect was really contributing little, if anything, to the relief of pressure in the posterior cranial fossa. In further simplification, therefore, the unilateral cerebellar approach is now proposed. It has been used in the last four tumors of this character and with no less satisfactory exposure of the tumor than with the bilateral approach. Unquestionably nothing can be worse than attempting to remove a tumor of the brain without providing adequate room not only for the existing intracranial pressure and the approach to the tumor but for all postoperative edema that develops. But it is also clear that all superfluous room is obtained at the cost of the patient's none too great physical reserve. If it is necessary to choose between too little and too much room, there can be no argument concerning the choice of the latter, but the best results are always obtainable by making the smallest approach that satisfies all needs. It will therefore be understood that, in suggesting the unilateral approach for cerebellopontile tumors, it is done with the full realization that inadequate provision for room is disastrous.

I might also add that obtaining room in the standardized fashion through a bilateral cerebellar decompression is in itself frequently most injurious to the contents of the posterior cranial fossa, i. e., the cerebellum and brain stem. I have in mind the great thrust backward of the cerebellum and brain stem when the dura is widely opened. The result of this is seen in the cerebellum, which is swollen from edema and internal hemorrhages and, symptomatically, from the patient's altered pulse and respirations. It is my feeling that many postoperative deaths are due to this injury inflicted early in the operation. By the unilateral approach only the outer part of the cerebellum on the operative side can be extruded, and this part is excised in preparation for the exposure of the tumor.

REDUCTION OF PRESSURE WITHIN POSTERIOR CRANIAL FOSSA

How, then, is the increased pressure within the posterior cranial fossa reduced to the point of safety?

Avertin Anesthesia.—First and perhaps most important is avertin anesthesia. Although the contents of the posterior cranial fossa are always under high pressure from three factors—(*a*) the tumor itself, (*b*) the internal hydrocephalus and (*c*) contiguous edema of the cerebellum and brain stem—an additional amount of pressure of variable but always important degree resulted when ether was used as an anesthetic. The absence of this effect with avertin has been commented

2. Cotterill, J. M.: Remarks on the Surgical Aspects of a Case of Cerebellopontine Tumor by Bruce, Tr. Med.-Chir. Soc., Edinburgh **18**:215, 1898-1899.

on elsewhere. It has greatly reduced the hazards of all operations for tumors of the brain and has also permitted the exposure of tumors by such smaller cranial defects. In hypophyseal tumors, for example, the opening in the bone is now one third or less than was required when ether was in use. The proposal to reduce the cerebellar approach to approximately one third of the former amount is only in keeping with the improvement made possible in hypophyseal operations. Without avertin as an anesthetic, the methods of space reduction that follow would doubtless be insufficient.

Tapping of a Lateral Ventricle.—When a lateral ventricle is tapped until the ventricular fluid ceases to flow, the supratentorial pressure is reduced to that of the atmosphere (fig. 1). This procedure, probably first introduced by Krause of Berlin, greatly relieves the pressure in the posterior cranial fossa. It is now quite generally used by surgeons in all operations for tumors below the tentorium. Without it all cerebellar operations would be dangerous when a high degree of pressure obtains. By gentle and steady pressure on the exposed dura an additional amount of fluid is obtained from the lateral ventricle, and in exactly this amount the subtentorial pressure is still further reduced. The latter method of relief must be used with great caution, for the pressure is likewise on the medulla, which above all else must not suffer. It might be added that in the unilateral approach the pressure is exerted more directly on the tentorium and less directly on the medulla than when all of the bone is removed in the bilateral exposure. Rather than incorporate the ventricular openings in a high occipital incision, as many operators prefer, I make two independent horizontal incisions (fig. 1 *A*), exactly as for ventriculography. By so doing the transverse incision can be made very low, i.e., below the inion, and a big, overhanging cutaneous flap can thus be avoided.

Evacuation of Fluid from the Cisterna Magna and Spinal Canal.—In nature's efforts toward space compensation for tumors in the posterior cranial fossa, the cerebellar tonsils are usually forced into the spinal canal, thus obliterating the cisterna magna entirely or in large degree. It might appear that this source of room, i.e., obtained by evacuating the fluid in the cisterna magna, which is of such great service in attacking the cranial nerves, would then be denied the operator on cerebellopontile tumors. The membranous roof of the cisterna is more difficult to reach, and the evacuation of the cisterna is not so spontaneous after it has been opened, but by gentle retraction on this part of the cerebellum the arachnoidal covering can be pricked and the tonsil elevated sufficiently (fig. 1) to permit the release of a large amount of fluid with proportionate covering of the pressure below the tentorium.

Excision of the Outer Cap of the Cerebellum.—This procedure is important in two ways: (*a*) It still further reduces any excess pressure within the posterior cranial fossa, and (*b*) the tumor is

exposed so that it may be attacked directly, i. e., without elevation of the cerebellum. Additional items of importance are (*c*) that postoperative edema of the cerebellar lobe from traction is avoided, and (*d*) that ample room is provided for any degree of postoperative edema that may ensue (fig. 1).

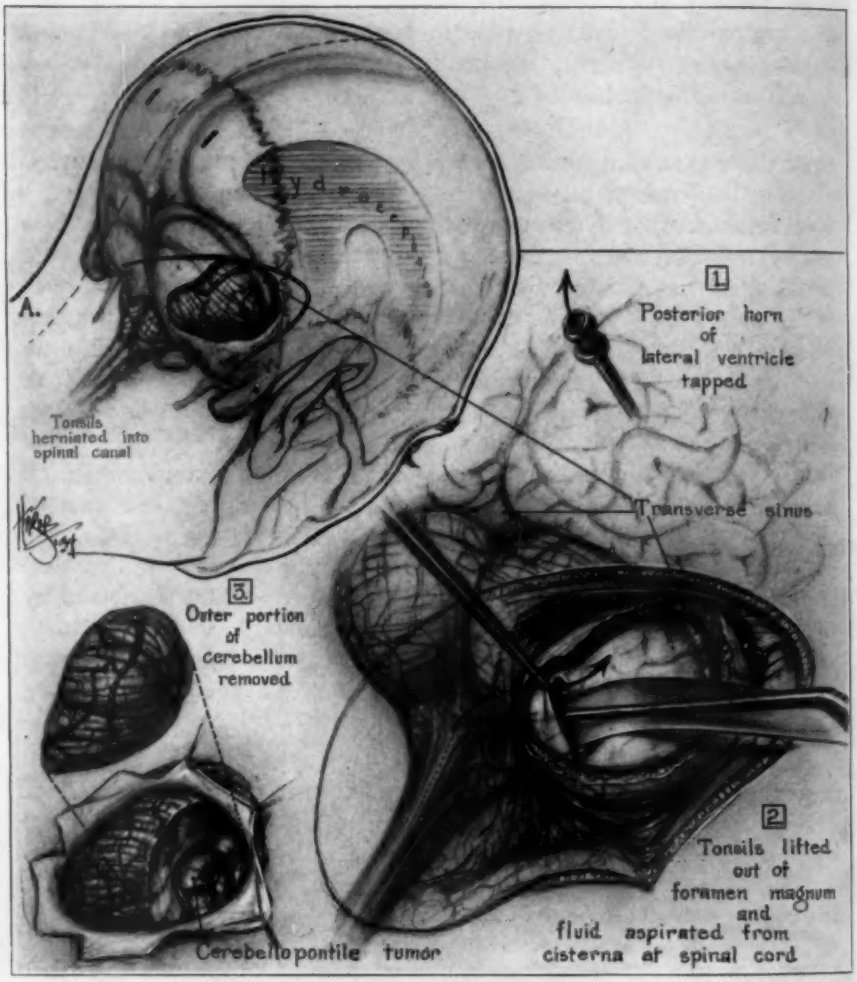

Fig. 1.—*A*, the relative exposure used in the removal of cerebellopontile tumors by the unilateral approach; *1*, the method of releasing the supratentorial pressure by puncture of the posterior horn of the lateral ventricle; *2*, further release of pressure in the posterior cranial fossa by evacuation of the cisterna magna in the spinal canal; *3*, final stage by the resection of the outer cap of the cerebellum.

Apparently there are no permanent effects from removal of this part of the cerebellum, the weight of which averages about 15 Gm. (fig. 4).

First suggested by Frazier [3] (1905), this method was rather harshly criticized at the time and until recently gained only a few adherents. It is an essential part of the unilateral operation. Cerebellopontile tumors can be removed by the bilateral operation without excision of the outer cap of the cerebellum, but even then to remove it makes the operation easier and the risk to life and function less. With the unilateral approach, removal of the tumor could hardly be attempted without this expedient. For its success the unilateral approach is indeed dependent on all of the methods of space reduction. It has been used in the last

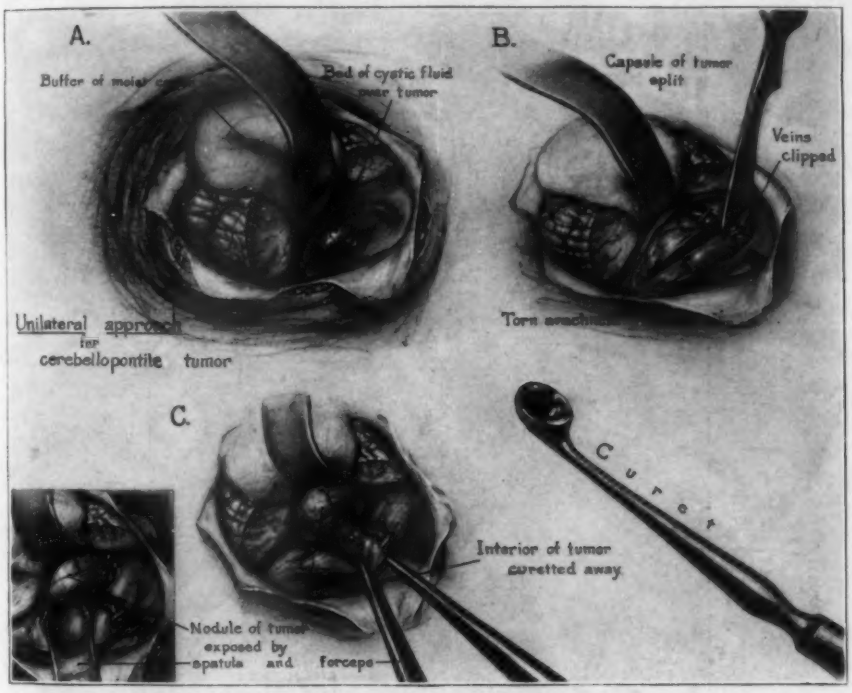

Fig. 2.—The method of attacking the tumor after the reduction of the intracranial pressure: *A*, exposure of the tumor; *B*, splitting the capsule of the tumor preparatory to intracapsular enucleation, and *C*, the gradual withdrawal of the capsule from its bed.

four cases, in each of which the tumor was totally removed according to the method of attack described elsewhere (figs. 2 and 5). For the past ten years I have strictly adhered to the policy of totally removing all tumors of this kind when seemingly possible, being firmly convinced that the operative mortality is not greater than by the partial removal and

3. Frazier, C. H.: Remarks upon the Surgical Aspects of Tumors of the Cerebellum, New York M. J. **81**:272 and 332, 1905.

that the postoperative course is smoother and more secure; never have I seen recurrence of such a growth as must always obtain when the interior of the tumor is removed. Three of the patients operated on by the unilateral approach are living and well. One of these was a decrepit woman, aged 62. Had a bilateral operation been performed, complete extirpation of the tumor would hardly have been possible. The last patient, who died, had the largest tumor of this type that I have seen (66 Gm.). She was comatose and badly dehydrated and had long

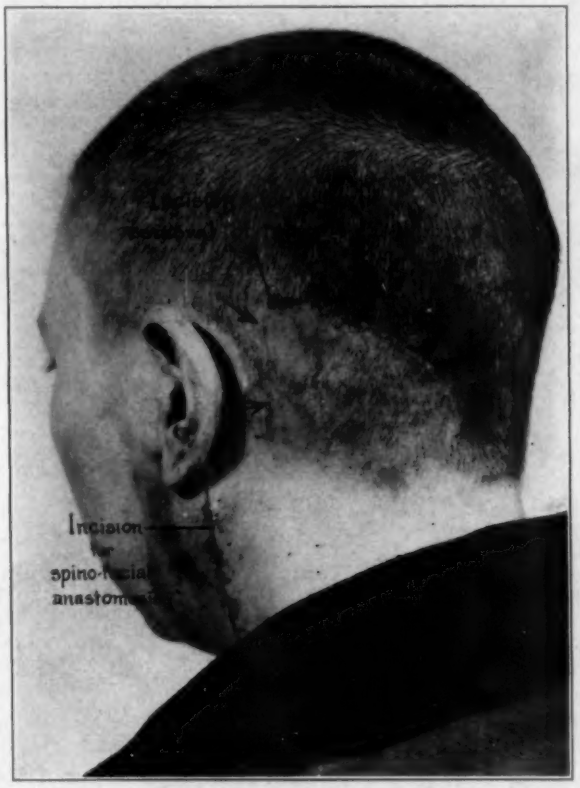

Fig. 3.—The operative scar following the removal of the acoustic tumor by the unilateral approach. Ten days after the tumor's extirpation a spinofacial anastomosis was made by an incision in the neck.

been blind. Earlier experiences were sufficient to prove that she could not survive a bilateral operation with complete removal or only partial extirpation. Up to the present comatose patients with cerebellopontile tumors have presented an insuperable problem. Perhaps with smaller tumors the unilateral approach may offer a degree of hope. Even with a tumor of this size the operative attack was at no time handicapped by lack of room or by intracranial pressure.

Fig. 4.—The outer cap of the cerebellum removed preparatory to the excision of an acoustic tumor which weighed 15 Gm.

Fig. 5.—Fragments of the interior tumor were removed with the curet, after which the remaining nubbin (the largest fragment) was gently withdrawn from its bed in the pons.

It cannot be claimed from this small series that a bilateral approach may never be indicated; certainly the need for it would appear to be exceptional. If the dural pressure is excessive after the release of ventricular fluid, one can continue the incision into the bilateral form without loss. The only difference between the unilateral approach used in trigeminal neuralgia or Ménière's disease and that in tumors of the cerebellopontile angles (fig. 3) is that the bony defect is increased somewhat toward the foramen magnum (fig. 1) in order to expose the restricted cisterna magna more easily, and toward the tentorium so that any tentorial vein may be safely thrombosed and divided when the cap of the cerebellum is being excised.

MYOKINETIC STUDIES OF TRANSPLANTED MUSCLES ABOUT THE KNEE

T. H. VINKE, M.D.
CINCINNATI

It is the purpose of this paper to present an accurate method of studying muscular contraction and its significance to gait in the normal person and after transplantation of muscles. The principles of these studies are found in Dr. Arthur Steindler's comprehensive lectures on myokinesiology and the work of Dr. R. Scherb. I shall briefly review the anatomy and physiology of the muscles of the thigh and outline the myokinesiology of the knee and the structures about it. These subjects are intimately related and are essential for an adequate discussion of transplantation of tendons. I have designed an instrument, the myokinesiometer, for the purpose of accurately recording muscular action in gait. The record obtained with the myokinesiometer shows the time and the extent of muscular contractions as compared with various phases of gait. I believe that the findings can be applied to orthopedic surgery, especially in cases of muscular imbalance as found in infantile and spastic paralysis. The myokinesiometer can be used for the examination of the majority of the muscles of the extremities. I have examined a series of normal persons and have compared my findings with those of Scherb. I have also examined a series of patients who have had transplantation of a tendon in the thigh. Observations were made to determine the action of the transplanted muscle and whether or not its action changed in relation to the gait after transplantation.

ANATOMY

In spite of the fact that the knee joint is large and has a large range of motion, it is remarkable for its stability. The large condyles of the femur articulate with the condyles of the tibia. The condyles are separated by two semilunar cartilages designed to produce a larger range of motion. The inner cartilage is C-shaped; its anterior and posterior horns are separated widely from each other in the midline; its posterior one half is firmly attached to the capsule; its anterior portion is attached near the crucial ligament and the anterior articular surface of the tibia. The external cartilage is circular; its two horns come closely together in the midline of the joint; it is not so firmly attached as the inner one,

From the service of Dr. Arthur Steindler, department of Orthopedic Surgery, University of Iowa, Iowa City.

and consequently it allows for a greater freedom of motion. These cartilages divide the joint into an upper and a lower half. The entire joint, including the patella, is enclosed in a large capsule. The capsule extends up on the anterior aspect of the femur to form a large pouch. The capsule is lined with synovia, which projects into the interior of the joint, anteriorly and posteriorly. The ligamentum mucosum and ligamentum alare are formed by the projection of prepatellar fat backward into the joint, which carries the synovia before it. The crucial ligaments push the synovia forward from the posterior aspect of the joint. The crucial ligaments are situated in the intercondyloid space.

The posterior crucial ligament runs from the posterior tibial spine to the median portion of the intercondyloid notch. The anterior crucial ligament runs from the anterior tibial spine to the lateral part of the intercondyloid notch. The anterior crucial ligament is longer than the posterior one. These ligaments aid in the stability of the knee by checking certain motions in all positions of the knee. The anterior crucial ligament becomes taut in extension, and the posterior crucial ligament becomes taut in extreme flexion. The lateral ligaments aid more in the stability of the knee than do the crucial ligaments.

On the anterior aspect of the thigh in the region of the knee is the quadriceps femoris. This muscle comprises a group of four: the (1) rectus femoris, (2) vastus lateralis, (3) vastus medialis and (4) vastus intermedius. The four muscles converge toward the patella and are inserted into the tubercle of the tibia. The patella is a sesamoid bone in the quadriceps tendon. Immediately above the knee the rectus femoris is superficial. The vasti lie on either side, and the vastus intermedius envelops the femur and is concealed by the other muscles. The rectus femoris has a double tendinous origin: (1) the straight head arises from the anterior inferior spine of the ilium, and (2) the reflected head arises from a rough groove on the dorsum ilii just above the highest part of the acetabulum. The vastus medialis arises from the distal two thirds of the linea aspera. The vastus intermedius arises from (1) the proximal two thirds of the body of the femur on the anterior and lateral surfaces and (2) the distal one half of the linea aspera.

The sartorius has its origin at the anterior superior spine and is inserted into the tibial tubercle.

The semitendinosus arises from the ischial tubercle and is inserted (1) into the medial side of the body of the tibia just distal to the medial condyle and (2) into the deep fascia of the leg.

The semimembranosus arises from the superior and lateral facet or the ischial tuberosity and is inserted into the horizontal groove on the posteromedial aspect of the medial condyle of the tibia.

The biceps femoris arises by its long head from the inferior and medial facet on the sciatic tuberosity and from the sacrotuberous liga-

ment. The short head arises from (1) the entire length of the lateral lip of the linea aspera and the proximal two thirds of the lateral epicondylic line of the femur and (2) the lateral intermuscular septum. The muscle is inserted into the head of the fibula.

The gracilis arises from the inferior ramus of the os pubis and is inserted into the medial surface of the body of the tibia just distal to the medial epicondyle.

In the cases studied in this report, the following principles of transplantation of tendons have been carefully observed:

1. Deformities should be corrected before transplantation by the breaking up of the adhesions and the severing of ligaments by means of a wedge resection or other operative procedure.

2. The mechanical arrangement of the transplanted tendon must be such that a straight line of pull is efficient, and the tendon acts in full force on its point of application.

3. All of the slack of the tendon should be taken up by applying sufficient tension when the joint is in the position of correction.

4. The anchorage of the tendon is important. The periosteal attachment is preferable to the tendon attachment.

5. The transplant should not be in contact with a bony surface, nor should it pass through a small hole in a fascial septum, because it will become adherent and interfere with movement.

6. The patient should be reeducated in the use of the transplanted muscle in its new position, or it may not function.

7. The choice of the proper muscle to be transplanted cannot be overemphasized. In acquired deformities the responsible cause is of significance whether it is spastic paralysis, infantile paralysis, partial paralysis, a stretched or contracted muscle or only a loss of muscular tone. With few exceptions, one group of muscles is paralyzed without other groups being affected.

Certain aspects of the function of muscle obviously concern transplantation, especially in its relation to kinetics. The function of the muscles depends to a large extent on the size, shape and direction of the muscle fibers as well as on the shape and length of the involved bones. The muscles have physiologically adapted themselves to physical requirements, such as speed and strength. The long, narrow muscle is adapted for speed, whereas the short, thick muscle is built for strength. Muscular action is modified further by various mechanical arrangements of the lever arm of the muscle, i. e., by changing the perpendicular distance from the point of application to the center of motion. Provided all of the other factors remain equal, a muscle will be capable of greater speed per unit of contraction if the muscle is attached close to

the joint. There is an example of this fact in the flexors of the knee. The flexors run parallel to the femur, and they are deflected in their course as they pass the posterior portion of the condyles of the femur. The lever arm of the muscles is changed because the condyles project considerably backward, and the tendons necessarily take on a much more diagonal direction just before the point of application of the leg is reached. In the case of the quadriceps femoris a sesamoid bone (the patella) is incorporated in its tendon, which makes a larger angle of application.

Muscles are arranged to work in groups, and the motion of the joint is dependent on normal functioning musculature. In the course of a muscle more than one joint may be involved. The hamstrings are polyarticular because they span the hip and the knee joints. The vasti muscles are monarticular, as they act on only the knee joint. The gastrocnemius is a polyarticular muscle arising from two heads, one on either side of the femur above the condyles. The muscles about the knee joint are long because they must accommodate the large range of motion of the knee, for the individual muscle fiber is able to contract only from one fourth to one half of its length in the relaxed position. In the upright standing position the knee joint maintains a position of inward rotation of 25 degrees against the head and neck of the femur and of 30 degrees against the lower end of the tibia. The normal range of motion is about 130 degrees, i. e., 50 degrees of flexion to from about 180 to 186 degrees of extension. Flexion and extension take place in the sagittal plane. In certain positions, the knee has a few degrees of inward and outward rotation.

Active insufficiency of the flexors of the knee joint as well as passive insufficiency of the quadriceps usually limits flexion. These conditions of the muscles are of importance in that they may influence treatment. The actual state of the muscle is accurately determined by myokinesiographic investigations.

The quadriceps muscles are essentially the only extensors of the knee joint. This action is chiefly accomplished by the vasti muscles. The tensor fasciae latae assists. The rectus femoris is not able to accomplish full extension under ordinary conditions. The extensor quadriceps is one of the most important stabilizers of the knee. When the knee is forcibly extended, the patella is drawn strongly upward by the quadriceps. The synovial lining and the fringes adhering to it are pulled out of the way of the condyles to prevent impingement. In this extended position the quadriceps muscles aid in stabilization. The anterior capsule is too large and loose to do so. The lateral ligaments of the knee assist greatly in the stabilization of this joint in extension because their posterior part becomes taut in this position. Abducent and adducent

movements of the tibia against the femur are checked by the lateral ligaments. These ligaments also check rotation when the knee is in extension, but when the knee is in flexion the lateral ligaments relax, and rotation is possible. During flexion the points of insertion of the lateral ligaments in the tibia and femur move closer together as the femur glides over the tibia. The lateral ligaments as well as the posterior capsule become loose, and rotary motion is possible. Rotary motion necessarily follows extension and flexion of the knee. In the beginning of flexion, the tibia is inwardly rotated against the femur. In extension the tibia is rotated outward in relation to the femur. In gait this is the case, for when the heel is placed on the ground, the pelvis swings forward, necessitating inward rotation of the thigh, for the foot cannot rotate while it is firmly planted on the ground. Naturally, if the femur is rotated inward, the tibia is rotated outward in relation to the femur. The inward rotation of the femur is primary, and the outward rotation secondary.

The action of the various muscles of the thigh is interesting, and a careful consideration of them is appropriate in this study. The action as compared to certain phases of gait will be considered later.

Contraction of the quadriceps tightens not only the tendinous insertion, pulling the patella upward, but also puts on tension of the entire anterior reenforcing apparatus of the knee, and thus aids considerably in the stabilization of the knee. The strength of the quadriceps is three times that of the combined hamstrings.

The hamstrings flex the knee joint, but they can extend the joint if the leg is fixed and the pelvis is free to move upward, causing the thigh to be extended against the leg.

The biceps act with a greater arm than do the inner hamstrings. The significance of this fact is that by so doing their action prevents a lockage of the knee when it is in full extension. Such lockage of the knee would occur if both muscles ran near the axis of the joint, in which case little or no rotation would develop in the muscles. The tendons of the hamstrings are inserted posteriorly, laterally and medially to the joint. The inner hamstrings rotate the knee inward. The outward rotation is accomplished chiefly by the tensor fasciae. These muscles must work with the utmost cooperation and efficiency. When one muscle contracts, its antagonist must relax. The relation of the actions of synergistic and antagonistic muscles are graphically illustrated by this myokinetic study. Scherb agrees with Codvilla in that the reciprocal action of the antagonists is controlled by the purpose of motion at the time of action. When a muscle is paralyzed, an interruption of the wave is experienced, and a transplantation is necessary to fill the gap. If the transplanted muscle takes the place of a synergist, it takes on a

synergistic action. A muscle may also be transplanted to take on the action of an antagonistic muscle. The opposite antagonist and agonist remain locked. One cannot take the place of another; they cannot fill their new function, which is strange to them in every phase of motion. It is evident that transplants depend not only on the mechanical and anatomic situations but also on the central nervous system. The myokinesiogram can demonstrate when a muscle takes on not only a new function but a compensatory action.

It is interesting and instructive to note that in the movement of any part of the body, in order to have proper coordination, the contraction of the muscles or group of muscles is regulated by two sets of stimuli: (1) those arising within the fibers producing the contraction, and (2) those arising in the fibers of the antagonist group which is supposed to relax the latter, in that way giving the former group the power to function properly. For instance, when the extensors of the knee contract, messages pass from their muscle spindles, not only to the quadriceps motor cells, but also to the motor cells which control the opponent group of muscles, the hamstring flexors. If there is to be no loss of power, the work of the opposing groups must be coordinated with the utmost nicety.

MYOKINETIC DATA

The choice of the distribution of muscular power by transplantation of a tendon should be made by kinetic investigation. This investigation must be accurately made, thereby determining the absence of individual muscles or muscular deficiency. A myokinetic study is necessary to obtain this required knowledge of muscular action of the lower extremities in relation to the action of these muscles to certain phases of gait. In studying myokinetics from a clinical standpoint, the principles of inspection and palpation are followed.

I have attempted to facilitate these observations by devising an instrument which I have named the myokinesiometer, constructed as follows:

The myokinesiometer makes use of the principle employed in the microphone button of a radio. A similar button was made for my purpose by using a small brass pill-box 1½ inches (3.81 cm.) in diameter and ½ inch (1.27 cm.) deep. A hole, 1 inch (2.54 cm.) in diameter, was made in the top of the box, and a mica window was placed inside. The mica window accommodates considerable motion and does not conduct electricity. A large flat copper terminal, 1 inch in diameter, was placed in both the top and the bottom of the box, with a terminal attached to the center of each. The terminals projected through the top and bottom of the box. The box was then filled with granulated carbon and closed. It was mounted on a small, light steel frame. Elastic bands, 18 inches (45.72 cm.) long, were muscles of the thigh. A lever, 6 inches (15.24 cm.) long, was fitted into the frame under the button so that the proximal end would press against the terminal attached to the frame, so that the box and the frame could be attached to the

when the distal end was pushed up. A bolt, 1½ inches long, was fitted into the distal end of the lever. The head of the bolt was one-half inch wide and made slightly concave, so that it was more adaptable for fitting against a tendon or muscle. The head of the bolt is the part of the myokinesiometer which receives the force of the muscle during contraction.

A slight pressure upward against the lever causes the lever to press against the bottom terminal. Variations in pressure against this button change the amount of current flowing through the button. The button with its frame is attached to the thigh by elastic bands. The elasticity of the bands is sufficient to prevent the influence of other muscles in the thigh (fig. 1).

By means of an electric wire, 25 feet (7.62 meters) in length, the myokinesiometer was attached to a polygraph. The magnetic field about the coil fluctuates in accordance with the variation of the current from the myokinesiometer. A small light steel rod was suspended in front of the coil. As the magnetic field

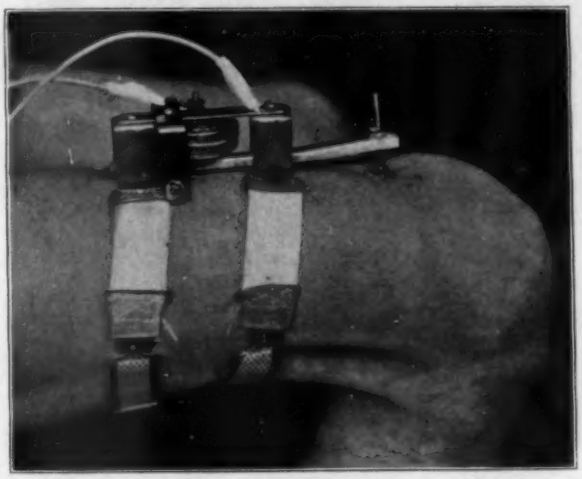

Fig. 1.—Myokinesiometer.

changes in intensity, the magnetic force is correspondingly altered. The steel rod is attracted according to the strength of the magnetic field. The greater the action of the muscle, the greater is the excursion of the rod. The steel rod was in turn connected to a recording pen on the polygraph. Three dry cells provide the electric current for the myokinesiometer and the recording device.

In this study I have used a procedure similar to the one used by Scherb in comparing muscular action with certain phases of gait. Scherb divided gait into two main phases: (1) the phase of double support or the period during which the subject stands on both feet and (2) the swinging phases, or the period during which the subject stands on one foot and swings the other. In normal gait, the following order occurs: (1) double support, (2) swing (left or right), (3) double support and (4) swing (right or left). A muscle usually acts during more than one phase. The period of double support is only momentary in ordinary

gait, and it is difficult without mechanical aid to observe just when these phases begin and end. For this purpose a Scherb sandal, with modifications necessary for the recording of the contractions, was constructed, as follows:

In the sole of the sandal I inserted two flat switches, one in the inside and the other in the outside of the sole. A third switch was inserted in the heel. The switch consisted of two pieces of tin 1½ inches square separated by thin rubber sheeting, care having been taken that the edges of the switch did not come in contact with each other. In the center of the switch a piece of rubber about one-half inch square was removed. This made it possible to close the switch by exerting a small amount of pressure over the switch, thereby bringing the two pieces of tin into close contact. When the pressure is removed the contact is broken. A signal magnet was provided for each separate switch. The switches were attached to the signal magnet by 25 feet of wire. This length of wire makes it possible for

Fig. 2.—Sandal with electric switches in the sole.

the subject to walk without danger of pulling the polygraph, with its attachments, from the table (fig. 2). Each signal magnet records the time the heel, the outer side of the sole and the inner side of the sole come in contact with the floor. The current from two dry cells operates the switches and the signal magnet.

By obtaining these records it is possible to determine the various phases of gait. If the sandal is worn on the right foot, the beginning of the right swinging phase is marked when the switch on the inner aspect of the sole is released. The end of the right swinging phase is recorded by the closing of the heel switch. The two double support periods and the left swinging phase occur between the right swinging phases. The periods of double support are only momentary and are not especially significant (fig. 3).

By the use of this instrument and method it is possible to record accurately the contractions of the muscles. I examined fifteen persons

with normal gait and compared my results with those of Scherb. It is obvious that it is impossible to examine all of the muscles, as they are covered by other structures such as the psoas, popliteus and small rotatory muscles of the hip. Only a few muscles remain active throughout the swinging phases. The sartorius is active throughout the entire swinging phase and from the time the heel touches the ground to the time all three points have touched. In the swinging motion the sartorius is an

Fig. 3.—Complete set-up of apparatus.

extensor, and in the support period it maintains extension but also holds itself in readiness as an external rotator as the heel touches the ground.

The curve of the gastrocnemius corresponds with the muscles of the thigh. It goes into action when the knee is flexed and when the heel begins to leave the floor.

All of these facts are shown on the myokinesiogram. Deficient muscles can be demonstrated by this procedure, and, of utmost importance, actual antagonists can be determined. The use of an antagonist muscle is always a doubtful procedure because of the difficulty of rear-

ranging impulses from the central nervous system. In order to decide on a transplantation procedure to replace a paralyzed muscle or to reenforce a weak or partially paralyzed muscle, one must determine the nature of the muscle to be transplanted. The myokinesiometer will be a great factor in the proper selection of the muscle for transplantation. With its use, accurate information regarding muscular action can be determined without undue influence of the examiner's judgment.

I shall first discuss a series of records of normal action of the muscles about the knee. The subjects chosen had no impairment in gait, and their muscular action was considered normal. A treadmill like the one Scherb used for his examinations was found to be a factor in producing abnormal gait; therefore it was successfully eliminated in this study. It was observed that subjects were afraid that they would fall from the treadmill when unsupported. A more serious objection to the treadmill was that the rate of gait was not determined by the patient but by the speed of the treadmill. The subjects in this series walked at their normal rate of speed. This was regarded as essential in the proper analysis of normal gait. The myokinesiometer was used in the study of all of these cases. The graphs obtained are shown in figures 4 to 10. Only the muscles about the right knee were examined. Figure 4 is a record of the normal biceps femoris; figure 5, of the normal inner hamstrings, and figure 6, of the normal quadriceps.

The three phases of gait were determined on the graphs. Since only one special sandal was used, it was possible to show definitely one phase of gait—the right swing. The other phases were mathematically determined. The period of right swing is shown on the graph by the space from the point where the switch under the inner side of the foot is released (line *C* on the graph) to the point where the switch in the heel is closed (line *B*). The making and breaking of the various switches in the shoe are indicated by notches in the respective lines on the graph. The line made by the heel switch extends in an opposite direction to that of the other two lines.

The periods between the phases of the right swing necessarily consist of two periods of double support and one of left swing. It is reasonable to assume that the period of the left swing is approximately of the same length as that of the right swing; therefore it covers about the same distance on the graph. If this distance (the length of the right swing) is measured in the space between the right swinging phases, the remaining distance is the length of the two periods of double support. Since there are two double supporting periods, the distance is divided by two, and the actual length of each double supporting period is known. These various periods have been designated on the graphs by vertical lines in the appropriate places.

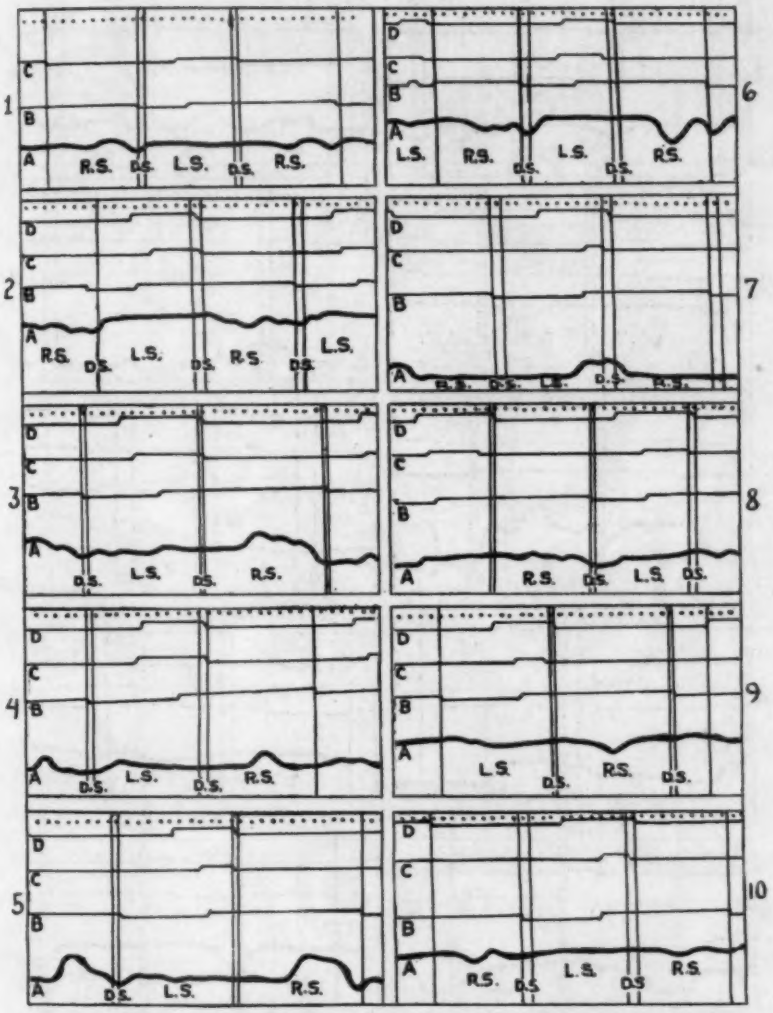

Fig. 4.—Myokinesiograms of normal biceps femoris: *A*, line showing the muscle contraction; *B*, line showing the time when the right heel is bearing weight; *C*, line showing the time when the forward outside portion of the foot is bearing weight, and *D*, line showing the time when the forward inside portion of the foot is bearing weight. In this and the remaining charts *D.S.* indicates double support; *R.S.*, the right swing, and *L.S.*, the left swing. The dotted line indicates the time interval; each space denotes one-tenth second.

The subjects in these examinations walked at a normal rate of speed. The period of double support is short in normal gait. In this series of cases it varied from 0.02 to 0.12 second. In Scherb's examinations

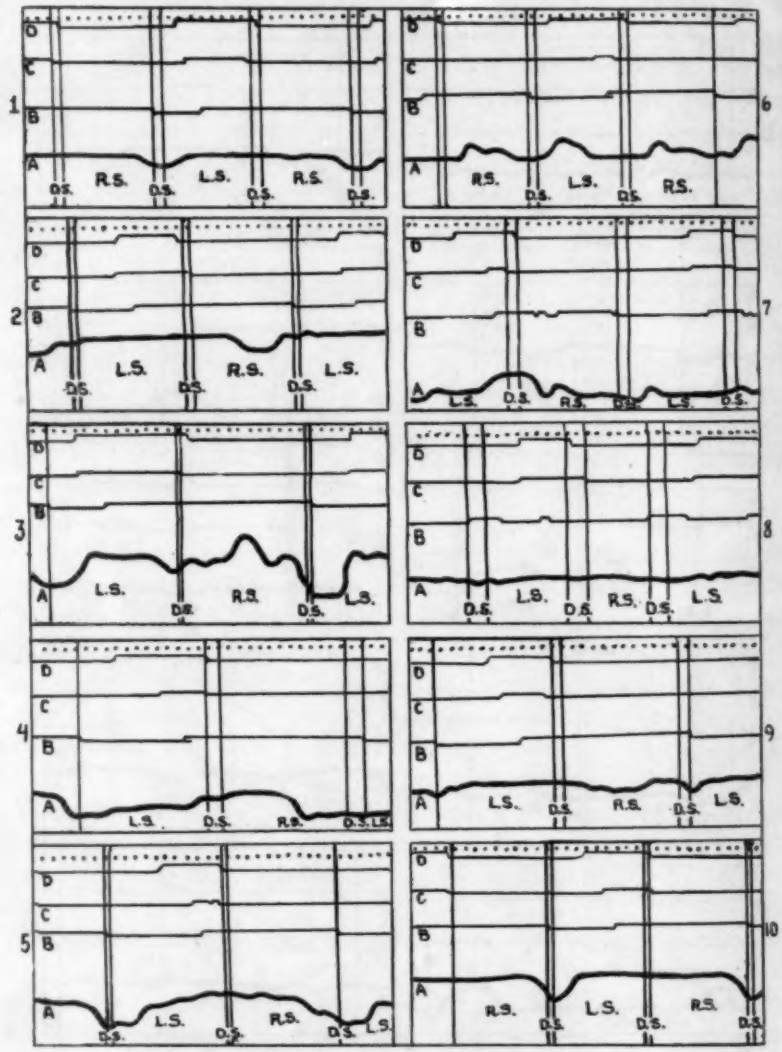

Fig. 5.—Myokinesiograms of the inner hamstrings.

the period of double support necessarily had to be longer, because his patients walked slowly in order that he might palpate properly; consequently the action in normal gait was unobtainable. There is a great deal of individual variation in muscular action, as shown by the myokinesiograms.

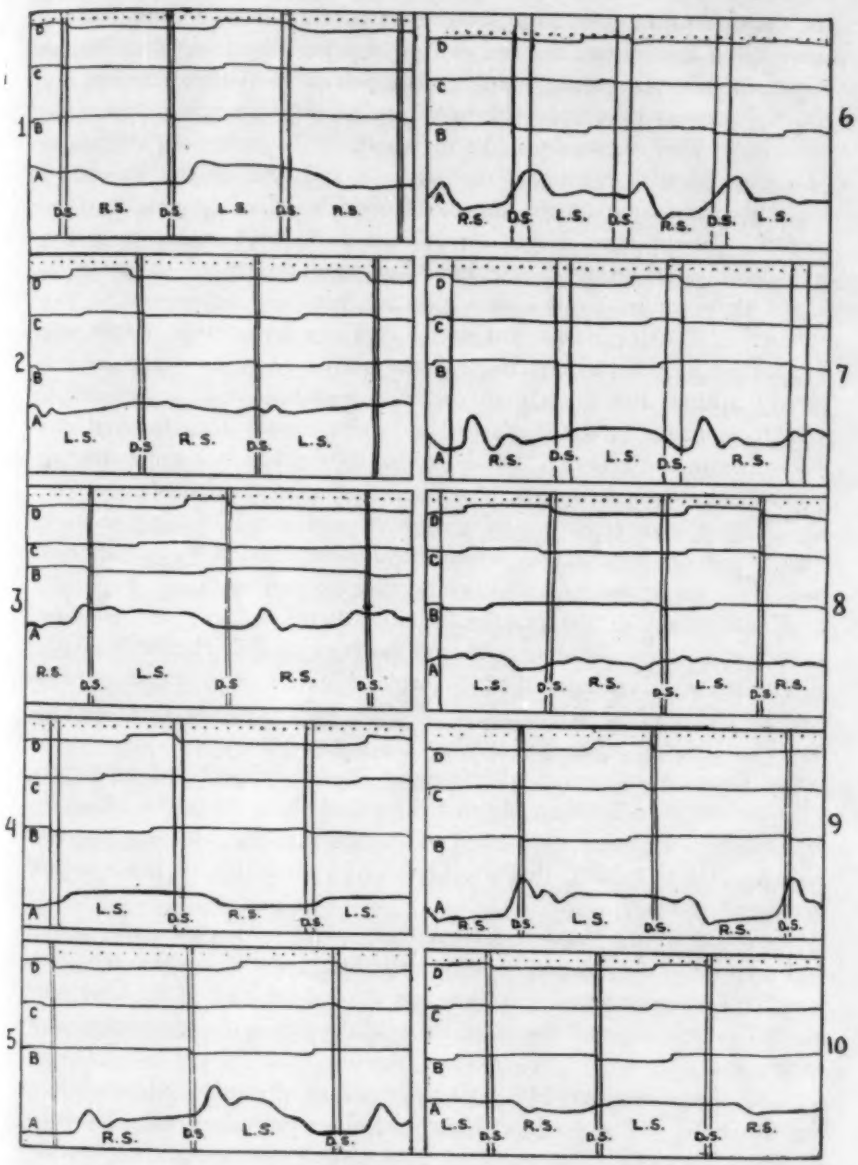

Fig. 6.—Myokinesiograms of the normal quadriceps.

In spite of the enormous individual variation, certain features characterize the individual muscles. It was found to be feasible to examine the quadriceps muscles as a group because they have a common insertion. The quadriceps relaxed during the period of right swing, and began to contract strongly during the period of double support after the right swing or during the first part of the left swing. Individual differences were shown by slight variations in the periods of contraction, as compared with certain phases of gait, and also by the intensity of the muscular action during the contraction wave. The period of time that the patient bore weight on various parts of his foot also varied considerably according to the individual and the speed of gait. The actual significance of this observation has not been determined.

Dr. J. T. McClintock suggested that the hamstrings might affect the record of contractions because the elastic band was fastened completely around the thigh. In order to evaluate this, I strapped the myokinesiometer to the thigh with adhesive tape. This resulted in no difference in the record. The elasticity of the bands around the thigh was sufficient to rule out the possible influence of the hamstrings.

The findings recorded by the myokinesiometer do not show the regular smooth contraction which Scherb determined by palpation but individual variations in intensity and time of action.

Examination of the gracilis, semimembranosus and semitendinosus gave results corresponding with the findings of Scherb, but individual variations were again marked. Graphs *3* and *8* in figure 5 show the extremes in individual contractions. The period of the muscular contractions usually began during the first part of the left swing and continued through the periods of left swing, double support and right swing. The period of relaxation began near the end of the right swing and was completed during the period of double support following the right swing. It was evident that the period of contraction of these muscles is extremely long.

Graph *8*, figure 5, shows a weak contraction. This particular subject had poor musculature, and consequently, little contraction is noted on the graph. The inner hamstrings acted as inward rotators of the knee joint, as well as flexors; under certain unusual conditions these muscles act as extensors.

The biceps relaxed only during the period of double support following the right swing in the majority of the cases observed. However, in a few cases relaxation occurred during the right swing. This follows Scherb's observations closely. The contraction acts over a long period of time, and is similar to that of the inner hamstrings in that it begins during the period of the left swing and continues through the period of double support and the right swing. It relaxes near the end of the right swing.

The hamstrings are synergists and in relation to certain phases of gait are similar in action. It is obvious that as far as muscular action alone is concerned, they could be interchanged by transplantation. The fact that the hamstrings can act as extensors under certain conditions and have a long period of contraction at the same time that the quadriceps muscles contract makes them suitable for transplantation to the quadriceps in cases of insufficiency of the extensor.

The foregoing records were taken in series and are not from selected cases. They represent a few of the variations that occur. Undoubtedly, if a large series of cases were examined, many interesting variations would be shown. What influence these variations have on normal gait and in transplantation of tendons can be determined only by careful study before and after transplantation.

Individual characteristics of muscular contraction can be determined only by delicate mechanical means and not by direct palpation, the method used by Scherb. These characteristics of muscular contractions are shown by the use of the myokinesiometer. A certain amount of care and technic must be used to obtain accuracy. The contact plate of the myokinesiometer must be placed directly over the muscle tendon. Furthermore, the plate must be adjusted so that with proper tension the slightest movement of the lever causes a motion of the recording pen.

A few patients who had had transplantations of tendons about the knee were examined in this manner with the myokinesiometer. One object of these examinations was to determine whether the transplanted muscle retained its original action in relation to gait or if it acquired the action of the muscle it replaced, thus the advisability of replacing a muscle by its antagonist. The records of cases of transplanted muscles are shown in figures 7 to 10.

In case 1 (figure 7) the right biceps femoris was transplanted to the quadriceps tendon. The insufficiency of the quadriceps was due to infantile paralysis. The biceps was unaffected by the disease. The action of the biceps was similar to its action in the normal position. The quadriceps worked strongly with the aid of this muscle. The inner hamstrings continued to act in their usual manner in spite of the fact that their synergist was transplanted. The patient also had considerable paralysis of the left leg, necessitating the use of a long brace. The patient walked with a marked limp, causing his gait to be slow, and therefore the period of double support was long. The period of right swing was about twice as long as that determined in normal gait. The top dotted line on the graph denotes the interval of time, each space denoting six-hundredths second, so that each swing lasted about 1.2 seconds. In spite of the slow, abnormal gait, the muscles retained a normal action in relation to gait. Although this patient still had a pathologic gait, the transplantation of the biceps caused marked improvement.

Case 2 (figure 8) was also one of infantile paralysis involving the quadriceps. The right tensor fasciae was transplanted to the weakened quadriceps. The transplanted muscle evidently aided little, if at all, for the action of the quadriceps continued to be weak. This patient had considerable shortening of the involved extremity. His gait was necessarily awkward. He compensated for his insufficient quadriceps action by swinging his entire lower extremity forward. The action of the

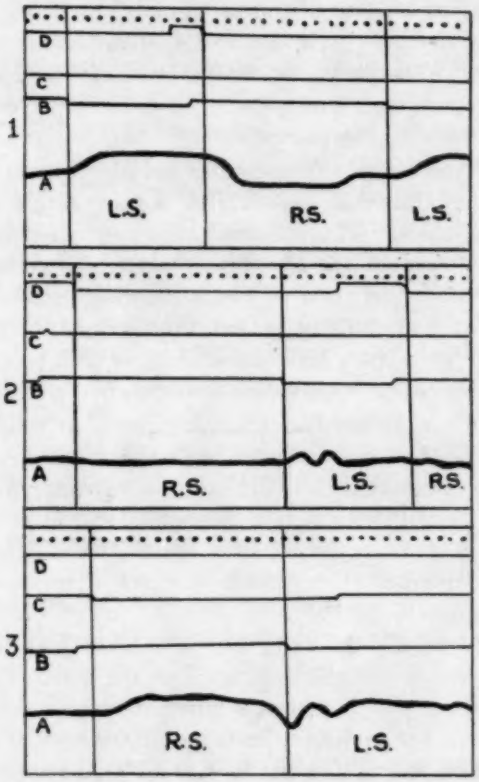

Fig. 7.—Myokinesiograms of the (*1*) biceps, (*2*) quadriceps and (*3*) the inner hamstrings following transplantation of the biceps transplanted to the quadriceps.

biceps femoris was abnormal in that a long period of relaxation occurred during the right swing. This apparently was a mechanism to facilitate the extension of the knee, showing that it can be changed under certain mechanical situations with the main characteristics of the muscular contraction wave remaining intact. It is, however, peculiar and perhaps contradictory to the foregoing statement that the inner hamstrings did not show a similar period of relaxation. The period of double support was not determined in this case, because the patient walked with a

smaller step on the right than he did on the left. In a case of this sort a sandal on each foot would be necessary to determine accurately the double supporting period. Transplantation of the tensor fasciae has been practically discontinued. This patient would have received more benefit, I believe, from a transplanted biceps femoris.

Case 3 (figure 9) was one of spastic hemiplegia. The right biceps femoris was transplanted to the insufficient quadriceps. Graph *A* shows

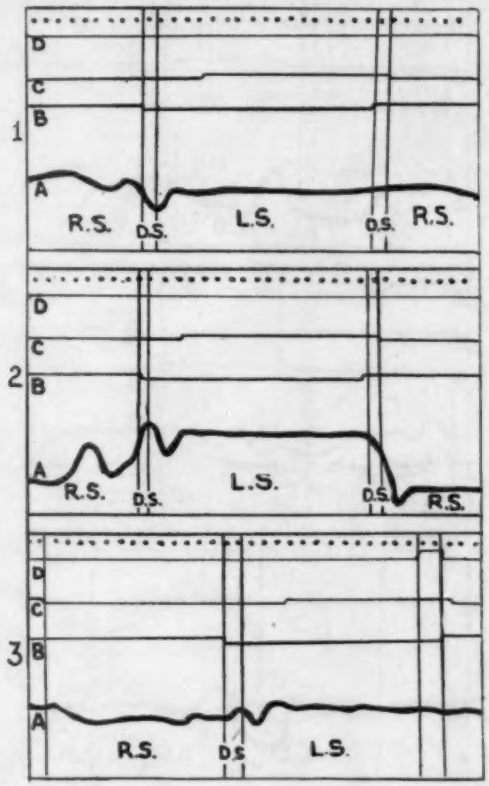

Fig. 8.—Myokinesiograms of the (*1*) biceps femoris, (*2*) quadriceps and (*3*) inner hamstrings following transplantation of the tensor fasciae to the quadriceps.

a relaxation between the right swing and the left swing, with a sharp contraction at the beginning of the left swing and no relaxation between the left swing and the right swing, including the period of double support. It is evident that a dissociation of muscular function did not occur. This, however, does not contraindicate transplantation, for the patient's gait was decidedly improved. The quadriceps action was strong. It is a matter of conjecture whether or not the small elevation

in the center of the quadriceps wave was due to the action of the biceps contraction, especially since it occurred at almost the same time that the biceps made a violent contraction. The inner hamstring showed a marked relaxation between the right swing and the left swing. This contraction wave was similar to that of the normal inner hamstring in case 3. The spasticity apparently did not make itself evident in the contraction wave.

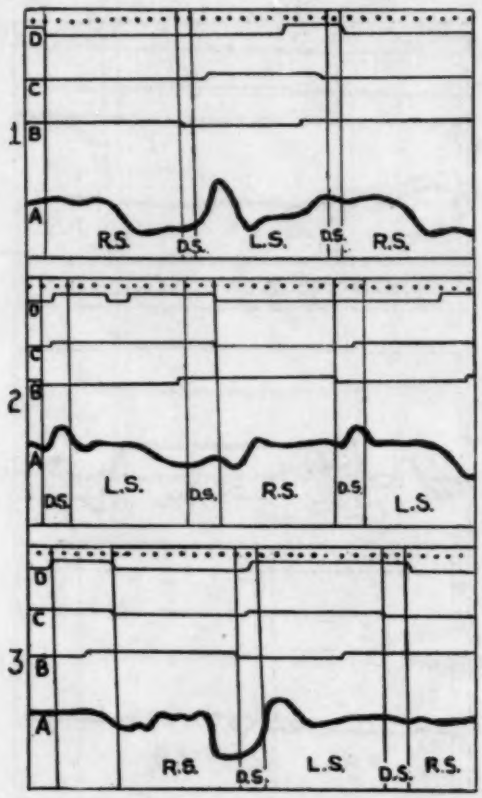

Fig. 9.—Myokinesiograms of the (*1*) biceps, (*2*) quadriceps and (*3*) inner hamstrings, following transplantation of the biceps femoris to the quadriceps.

Case 4 (figure 10) was another instance of spastic paralysis. The left biceps femoris was transplanted to the quadriceps. The biceps again showed the usual contraction wave, and this fact further supports the contention that dissociation does not take place. The quadriceps showed a rather weak contraction wave in spite of the fact that it was aided by a transplanted muscle. The patient felt certain that the operation had markedly improved her gait. The inner hamstrings had a more or less

normal action. The patient walked with both legs inwardly rotated and with slight flexion of the hip joints.

It is unfortunate that more patients were not available for examination in this study. In view of the small number of cases, sweeping conclusions cannot be made. Nevertheless, evidence has been obtained that the transplanted muscles retain their original or nearly their original contraction wave after transplantation. These factors are of importance

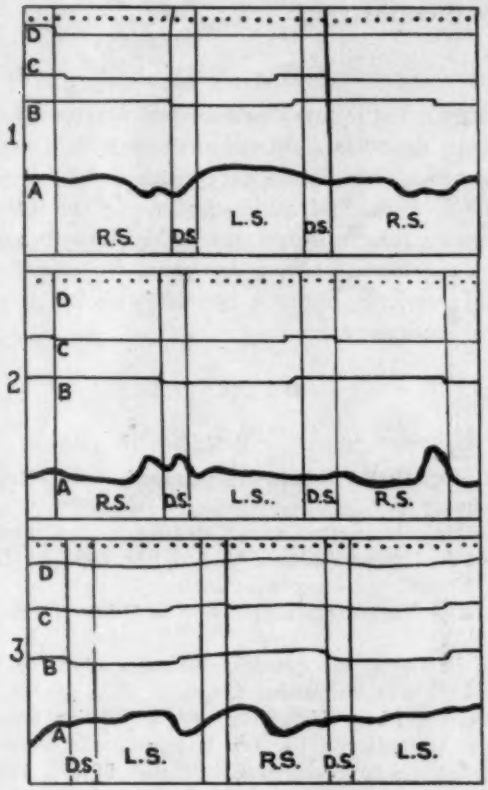

Fig. 10.—Myokinesiograms of the (*1*) biceps femoris, (*2*) quadriceps, and (*3*) inner hamstrings following transplantation of the biceps femoris to the quadriceps.

in transplantation of tendons and muscles, for it is obvious that if a muscle retains its original action in relation to certain phases of gait, it will be the muscle of choice for the replacement of a similarly acting insufficient or paralyzed muscle. The study of transplantation of muscles in both spastic and infantile paralysis shows that the biceps femoris can be transplanted to the quadriceps with good clinical results. Normally, the biceps femoris contracts during the left swing at the same time that the quadriceps acts; therefore, when the biceps femoris is

transplanted, it definitely aids the action of the quadriceps, in spite of the fact that its original action continues.

Isometric contractions make themselves evident in the records obtained by the use of the pill-box myokinesiometer, although from a purely theoretical basis this is not possible. In isometric contractions, a certain amount of slack and elasticity must be absorbed before the tendon is taut. When the tendon changes from a relaxed to a taut condition, or vice versa, enough motion takes place in the muscle or tendon to make a record on the graph.

CONCLUSION

A new instrument, the myokinesiometer, for the study of muscular function, has been described. In conjunction with this device, a sandal with special electrical switches was constructed to determine various phases of gait. The method outlined is useful in making the proper selection of muscles for transplantation. Myokinesiograms obtained by the use of this apparatus show a variation in muscular contractions. Other points of academic interest can likewise be determined by the use of the myokinesiometer.

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INTUSSUSCEPTION IN INFANCY AND CHILDHOOD

A REPORT OF THREE HUNDRED AND SEVENTY-TWO CASES

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During the twenty-five year period from 1908 to 1932, inclusive, 121,515 patients were admitted to the wards and private wing of the Children's Hospital, Boston, and in this time 372 cases of intussusception were encountered. This report is based on a study of these 372 cases. In order to show the improvement in treatment of intussusception, analyses have been made for the first twenty year period, from 1908 to 1927, as contrasted with the last five year period, from 1928 to 1932. References were made to 63 of these cases in 1915 (Ladd) and to an additional 99 in 1925 (Ladd and Cutler).

INCIDENCE ACCORDING TO AGE AND SEX

Eighty-seven per cent of the cases occurred in children under 2 years of age, and 70 per cent in children between the ages of 4 and 11 months, with the peak of incidence in those at 7 months. The youngest patient was 17 days old, and the oldest of the series was aged 11 years. Table 1

TABLE 1.—*Incidence According to Age (372 Cases)*

Age	Cases	Age	Cases	Age	Cases	Age	Cases
1 month.....	1	10 months.....	23	19 months.....	5	4 to 5 years...	11
2 months.....	8	11 months.....	16	20 months.....	3	5 to 6 years...	5
3 months.....	10	12 months.....	4	21 months.....	2	6 to 7 years...	3
4 months.....	27	13 months.....	8	22 months.....	3	7 to 8 years...	2
5 months.....	44	14 months.....	3	23 months.....	1	8 to 9 years...	2
6 months.....	46	15 months.....	2	24 months.....	3	9 to 10 years...	1
7 months.....	50	16 months.....	3	2 to 3 years....	12	10 to 11 years...	1
8 months.....	32	17 months.....	2	3 to 4 years....	11	11 to 12 years...	0
9 months.....	25	18 months.....	3				

shows the distribution of the cases in age groups, and figure 1 graphically illustrates these statistics. Figure 2 shows the distribution of cases in the group under 18 months of age. The condition was found to be more common in boys than in girls, the proportion being 226 boys (61 per cent) to 146 girls (39 per cent).

From the surgical service of the Children's Hospital.

PATHOGENESIS

Unfortunately, from the study of our material, no contribution has been made to the knowledge of the pathogenesis of intussusception. Some of the invaginations were caused by inverted Meckel's diverticula (14 cases), intestinal polyps (2 cases), enterocyst (1 case), lymphoma

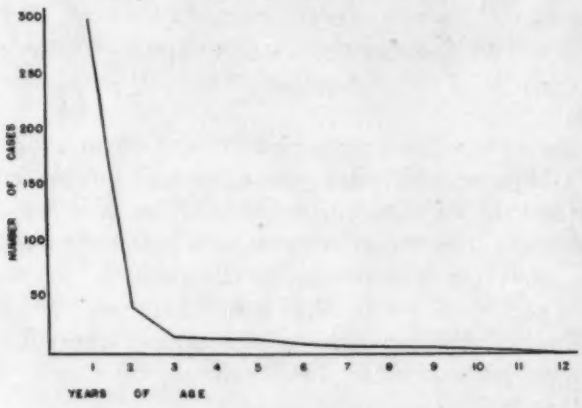

Fig. 1.—The distribution of 372 cases according to age.

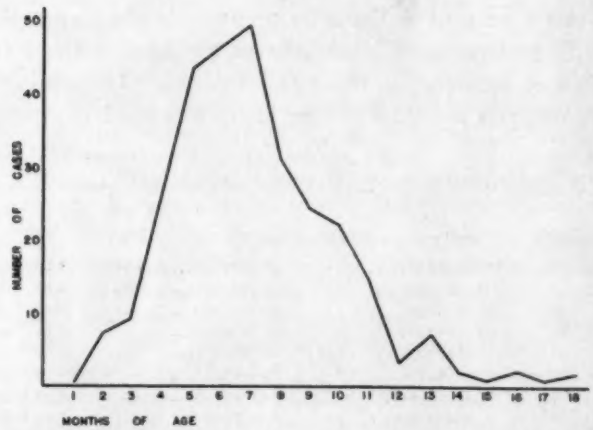

Fig. 2.—The distribution of 307 cases according to age in the group under 18 months old.

of the ileum (1 case) or other lesions of the bowel. Yet these cases comprised only 5 per cent of the series. This leaves a large group in which there was failure to detect the causal factor.

Fraser mentioned that intussusception is commonest among children of the poor because errors in diet are most frequent in this class. Our

studies do not support his contention, for the incidence in patients who entered the private wing was approximately the same as in those who entered the public wards. In addition, the condition occurred most frequently in well developed and well nourished infants—obviously not those in whom dietary errors were common.

Several tabulations appear in the literature which show a slightly higher incidence in December and in either April or May, presumably because festivities around Christmas and Easter lead to dietary indiscretions. However, no appreciable increase during these seasons was found in our series.

No familial tendency was noted, for in only two families was there a second case of intussusception.

TABLE 2.—*Types of Intussusception in 372 Cases*

Type of Intussusception	Cases, per Cent
Ileo-ileal (enteric)	7
Ileocolic	75
Ileo-ileocolic	9
Colocolic	2
Type not stated	7
Multiple intussusception	(3 cases)
Retrograde intussusception	(1 case)

TABLE 3.—*Points of Origin of Intussusception in 372 Cases*

Leading Point	Cases	
	Number	Percentage
Ileum—above the distal 1 foot	60	16
Terminal ileum, ileocecal valve and cecum	274	74
Ascending colon	6	1.6
Hepatic flexure	5	1.3
Leading point not stated	27	0.7

In 7 cases, intussusception occurred as a sequel to dysentery or infectious diarrhea.

TYPES OF INTUSSUSCEPTION

Intussusceptions were listed as ileo-ileal (enteric), ileocolic (fig. 3), ileo-ileocolic and colocolic, depending on the point of origin and the position to which the intsussusceptum had progressed.[1] The ileo-ileocolic form is that in which the ileum telescopes into itself first, after which the terminal portion of the ileum passes into the colon from a second leading point. A retrograde intussusception is said to occur only at the time of death or impending death, but we have had 1 case of ileal retrograde intussusception with recovery. Table 2 shows the

1. The intussusceptum is the invaginated portion, and the intussuscipiens is that part which receives the intussusceptum.

frequency of occurrence of the various forms and table 3 the points of origin.

SYMPTOMS

In this series of cases of acute intussusception the onset of symptoms was characteristically sudden, and the mother could usually tell the exact time at which the child was taken sick. In a typical case, the infant while in excellent health suddenly cried out in extreme pain,

Fig. 3.—A specimen of the common type of ileocolic intussusception, showing the ileum telescoped into the ascending colon: *A*, appendix; *C*, ascending colon: *I*, intussusceptum (ileum).

"doubled up," turned pale, sweated and vomited soon afterward. Such a paroxysm lasted for a minute or two, and was followed by a period of relief. The attacks recurred at intervals of from ten to fifteen minutes. Between attacks the child went to sleep or was playful and without complaint. In 82 per cent of the cases in this series there was a manifestation of pain, in 90 per cent there was vomiting, and in a high percentage there were sweating and pallor. Fever, however, was a less

common symptom, and its presence was indicative of long-continued vomiting and dehydration.

Blood appeared in the stools in 88 per cent of the cases within twenty-four hours after the onset of symptoms. The first stool after the beginning of the illness was often normal, since it represented an evacuation of material that previously had filled the rectum. Later stools contained mucus, mucus and blood or unmixed blood.

The history usually suggested the correct diagnosis. However, when the child was seen in the early stages and between the paroxysms of pain and vomiting, his healthy appearance tended to make one disregard the story of the parent. Hence it was found that the history was very important whether or not the child looked sick.

In the chronic and subacute forms of intussusception, pain was a less prominent feature, but was usually the chief complaint. Blood was often absent from the stools. Because of infrequent vomiting, dehydration was slight or absent. While the symptoms were of relatively long standing, their mildness was demonstrated by the fact that the patients often continued in fairly good health.

PHYSICAL FINDINGS

One of the most characteristic findings of intussusception in this study was its frequent occurrence in a well nourished and well developed child. However, by the time the patient was seen in the hospital, he was pale and listless though in a good state of nutrition. When vomiting was of long standing, dehydration was present. In about one tenth of the cases the condition of shock was marked. Twenty patients were classified as moribund on entry and were in such extremity that 9 died before operation could be performed, and 4 others died during the course of immediate laparotomy.

In 312 cases (84 per cent of the series) abdominal examination revealed the presence of a mass. This was poorly defined in some instances, but was usually a discrete, rounded or sausage-shaped tumor. The mass was rather firm and was not tender (tender in only 6 instances). Occasionally it was felt to increase in hardness during the attacks of pain. Since the great majority of the intestinal invaginations had proceeded into the colon the mass was found along the course of that organ. When the intussusceptum was in the hepatic flexure, it was sometimes difficult to detect because of the overlying liver. Palpation of the mass in the epigastrium or on the left side of the abdomen, indicating an advanced intussusception, was at times accompanied by an "empty" right lower quadrant of the abdomen (Dance's sign) because of the invagination of the cecum up into the colon.

When the history was suggestive of intussusception and when abdominal examination was unsatisfactory because of distention or because the child was fretful and uncooperative, we made it a rule to make an immediate examination under ether anesthesia. Before the examination was made, however, all preparations were completed for an immediate laparotomy. In 10 cases the tumor was felt only after the patient was thus anesthetized.

The palpation of the intussusceptum within the rectal lumen in 106 cases (28 per cent of the series) showed the value and importance of rectal examination. When felt with the examining finger, the advancing portion of the bowel had the general shape of an adult cervix uteri. Even though the tip of the advancing mass was not always encountered in the rectum, bimanual examination occasionally revealed a tumor higher up in the peritoneal cavity, which would have eluded detection by abdominal palpation alone. Shelley recommended bimanual palpation with the baby held in a sitting posture, because the tumor will then usually drop down between the examiner's fingers. In 4 cases the intussusceptum had proceeded so far that it protruded from the anus; in 2 of these cases the children were referred for "treatment of prolapsed rectum." The differentiation between intussusception and prolapsed rectum could be made rapidly by passing the finger into the rectum between the intussusceptum and the surrounding anal sphincter. In prolapse of the rectum there is no such space to admit a finger.

After withdrawal of the examining finger blood was detected in 183 cases (50 per cent). In 11 of these no suggestion of rectal bleeding had been noted in the history. The blood appeared to be undiluted, intermingled with mucus or admixed with feces. Often it was described as appearing similar to prune juice.

Fever was absent in patients brought to the hospital soon after the appearance of symptoms, but was present in those who had had symptoms long enough to become dehydrated.

ROENTGENOGRAPHIC OBSERVATIONS

In the typical cases of acute intussusception, which formed the majority of this series, the history and physical findings led to a positive diagnosis and made roentgenographic studies unnecessary. There were, however, a minority of cases in which the symptoms or signs were atypical leaving the diagnosis doubtful. In this group an enema of barium sulphate, with fluoroscopic and roentgenographic studies, was a valuable aid. In 17 such instances 16 positive diagnoses were made by roentgenograms and confirmed by immediate laparotomy; in 1 case (ileo-ileal type) the roentgenographic findings were normal, but an intussusception was found at operation.

The main, typical observations made at roentgen examination following a barium enema in ileocolic intussusception were: (1) obstruction to the injection of barium; (2) a cupola effect or cupping in the head of the barium as it met the intussusceptum; (3) a thin cylindric shell of barium around the intussusceptum (and inside the intussuscipiens); (4) possibly a palpable tumor at the site of obstruction, and (5) a remaining cylindric shell of barium surrounding and outlining the intussusceptum after evacuation of the enema.

Lehmann, in 1913, reported the first observations on detection of an intussusception by barium enema and roentgenogram, while Ashbury,

Fig. 4.—Roentgenograms made after the administration of a barium enema. In the film on the left, a filling defect is shown in the right half of the transverse colon. In the film on the right, taken after evacuation, the barium is shown remaining around and outlining the intussusceptum in the hepatic flexure and the right half of the transverse part of the colon. The accumulations of gas in the right flank are indicative of intestinal obstruction.

Stephens, Sussman and others treated this subject more fully in their respective articles.

TREATMENT

In 1874 Hutchinson performed the first abdominal section with successful reduction of an intussusception, and since that time the treatment of this condition has tended toward operative intervention. In spite of the almost universal adoption of surgical treatment, there have been

several published reports, notably those of Hipsley, Kock and Oerum and Monrad, which favored the method of reduction by colonic injection of fluids. Arntzen and Helsted, Retan and Stephens advocated reduction by the injection of a barium enema under fluoroscopic observation. We are opposed to all such methods of reduction by colonic inflation. In those clinics in which this type of treatment is employed, a considerable number of the cases come to operation because of irreducibility or to make certain that complete reduction has been effected. Operation is therefore necessarily delayed, and the child is subjected to a procedure which depletes its narrow margin of reserve. By limiting ourselves to operative treatment a simplification resulted which appreciably aided in reducing the mortality.

Various surgeons have employed the following types of operations: (1) reduction; (2) resection with anastomosis; (3) resection with double enterostomy (Mikulicz); (4) removal of intussusceptum through incision in intussuscipiens (method of Coffey, Maunsell or Jessett); (5) anastomosis around the mass, leaving the intussusceptum to slough out; (6) anastomosis around the mass and resection of the intussusceptum at a second operation, and (7) ileostomy, with resection at a second operation.

Our series included examples of each of these except the last two.

Since intussusception has been regarded as an urgent surgical emergency it has been our practice to perform laparotomy immediately. The average patient was admitted, operated on and put to bed within from forty to fifty minutes. When dehydration was marked, parenteral fluids were given before operation. The time required to admit, give dextrose intravenously and saline solution subcutaneously, and be ready for operation was rarely more than thirty minutes.

The anesthetic used in all cases was ether. In some of the earlier operations an incision in the midline of the lower part of the abdomen was made, but since then a right paramedian rectus incision has been commonly employed, because the most difficult part of the reduction occurred in the region of the cecum or lower part of the ileum. Hence the incision was not made over the palpable tumor unless the mass happened to be in the right lower quadrant of the abdomen.

As far as possible reduction was performed intra-abdominally. This was done by a process of milking back, or "taxis," by putting gentle pressure over the intussuscipiens with the hand and squeezing out the invaginated part. Unfortunate experience has shown that the intussusceptum should never be pulled out, for if the intestine is friable, a rupture and peritoneal soiling result. In the region of the cecum and ileum the reduction often became difficult or impossible, and at this stage the mass would be delivered outside the abdomen. Continued

annular pressure with the hand and a stretching of the receiving ring usually reduced the edema enough to allow complete reduction. Application of hot isotonic saline solution during the manipulation aided the reduction. An intestine that looked bluish, discolored and of questionable viability often improved in a few minutes.

In recent years attempts at reduction have been persisted in more than formerly, for continuance of this procedure was often successful, whereas early recourse to resection would undoubtedly have resulted in more fatalities. Not infrequently the serosa was accidentally split as much as 6 inches (15 cm.), but this did not prove to be a serious complication. A few quickly placed stitches of silk or fine catgut sufficed to bring the serosal edges together. Brown suggested deliberate incision of the serosa to permit reduction.

Reduction was effected in 308 cases (83 per cent), with a mortality of 27 per cent in the first twenty year period as compared with 12 per cent in the last five years. In conjunction with reduction the following procedures were done as indicated: 1. The ileum was drained in 9 cases when the intestine was of doubtful viability. In 2 of these, this was accomplished by opening a Meckel diverticulum. 2. In 7 other cases a Meckel diverticulum was excised. 3. In 13 cases the appendix was removed. 4. In 1 case the terminal part of the ileum was sutured down to the parietal part of the peritoneum in an attempt to prevent recurrence.

An appendectomy was performed twelve times during the first twenty year period, but only once during the last five years, for we have come to believe that nothing more should be done than is absolutely necessary. While removal of the appendix requires only a few minutes, it is an additional trauma which may lead to death in children who are extremely ill. Involvement of the appendix in the intussusception makes it reddened and swollen, but this condition must not be confused with appendicitis. Various authors have reported that they removed the appendix as a routine, believing that irritation from appendicitis induced the spasm which brought about the invagination. We place little credence in this view and do not believe that the appendix should be removed unless it is gangrenous or its vessels are thrombosed.

In babies under 1 year of age resection of intussusception has carried a high mortality. In 1921 Clubbe reported 2 successful resections and collected 17 instances from the literature. He did not include the reports of Eisendrath and of Frank—the latter being the first to perform and record a successful resection in an infant in this country. Without exhaustive search, 6 cases have been found recorded since 1921, bringing the total to at least 30. Clubbe performed the first successful resection in 1896. Robbins reported the most extensive resection, with

removal of the terminal part of the ileum, the cecum, the ascending colon, the transverse colon and a portion of the descending colon, followed by a successful ileosigmoidostomy. Dowd, in operating on a 5 day old infant, performed a successful resection in the youngest patient on record for this operation. But, as has been pointed out, reduction of the mortality lies not so much in improvement in the technic of resection as it does in obtaining cases before resection is necessary.

In our series 30 resections were done; in 16 there was an ileocolostomy, with 1 recovery, and in 14 there was a double enterostomy (Mikulicz' procedure), with 1 recovery. The 2 recoveries were in 4 year old boys, 1 with symptoms for twenty-four hours and the other

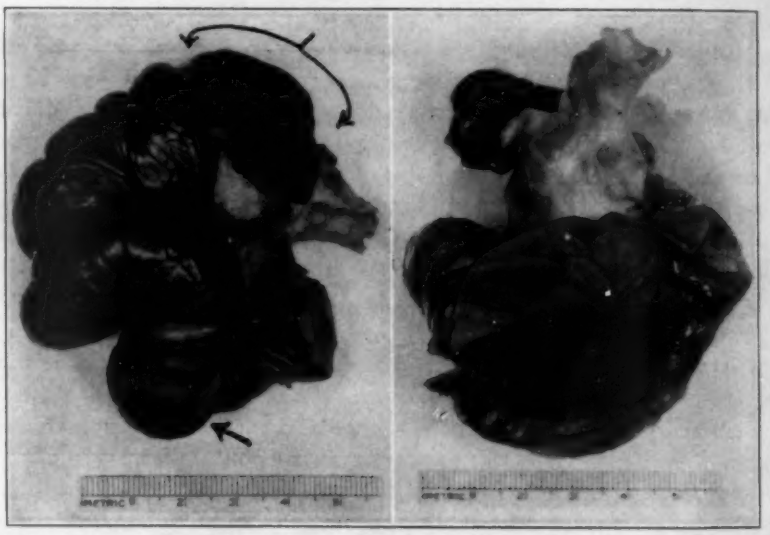

Fig. 5.—A specimen of an irreducible intussusception. In the photograph on the left the bracket at the top points out the ileum as it telescopes into the terminal part of the ileum, and the arrow at the bottom indicates the position to which the intussusceptum has advanced. The photograph on the right shows the lower portion of the ileum cut open to permit a view of the gangrenous leading point.

with symptoms for three days.[2] When resection was necessary, a double enterostomy was regarded as preferable to an anastomosis, though we have no figures to support the contention.

2. Since completion of this article there has been a third successful resection with establishment of a double enterostomy. This was in a 4 month old boy who had had symptoms for forty-eight hours. One of us (W. E. L.) has performed an additional successful resection at another hospital, which is not included in this series. This was in a 3 year old child, in whom a lateral anastomosis was performed.

In 3 instances of unsuccessful resection with ileocolostomy the method used was that of Jesset or of Maunsell; that is: (1) sewing the invaginating portion to the intussuscipiens with stitches placed around the ring or neck of entry; (2) making a longitudinal incision in the intussuscipiens (just distal to the line of suture), and (3) cutting off and removing the intussusceptum through this opening. The incision was used as an enterostomy in 2 cases.

In 1906 Rutherford first employed an anastomosis—ileocolostomy—around the undisturbed mass, and Parry and Bullock reported such operations in 1909 and 1920, respectively. Montgomery and Mussil, in 1930, listed two successes with this short-circuiting operation, and substantiated their work by experiments on animals. We have had experience with this procedure in only 1 case. The patient had an irreducible intussusception which originated from an intestinal lymphoma. He recovered without event, but whether or not the intussusceptum sloughed out is not known, for it was never identified in the stool. The patient was discharged with the intestinal obstruction relieved, but died three months later from a massive abdominal extension of the lymphoma.

It is important to note that there have been fewer resections in the last five years, there being only 2 in the last 90 cases (2.2 per cent) as compared with 28 in the previous 282 cases (10 per cent). This reduction was due to three factors: First, in the last five years patients were referred earlier for treatment. Second, we became somewhat more bold in attempting and completing reductions which previously would have been termed irreducible. Third, experience showed that the intestine, though badly discolored and damaged after reduction, was frequently viable, whereas formerly such an appearance would have led to resection.

Because of the high mortality resulting from reduction of an intussusception and excision of a Meckel diverticulum at the same operation (5 deaths in 7 attempts), it was better, when possible, to leave the diverticulum till a second operation so that it could be removed with more safety (no deaths in 3 cases).

In 16 cases the intussusception was found to be wholly or partially reduced at operation. In all these cases the symptoms and physical findings had been unquestionable, and in each instance there was vascular congestion with edema in the terminal part of the ileum, the cecum and the ascending colon, which was interpreted as evidence of recent intussusception. Such a finding represents either a spontaneous reduction or a reduction attendant on manipulation at examination.

The mortality in our series during the last twenty-five years has taken a continuous marked downward trend from 59 per cent in the first five years to 14 per cent in the last five years (fig. 6).

FACTORS IN MORTALITY

The most important factor in reducing the mortality in intussusception is a reduction of the time between the onset of symptoms and the operation. This point has been demonstrated amply in other clinics and communities and too much credit cannot be given to Clubbe, Hipsley and other surgeons of Australia, who brought the mortality to amazingly low limits by persuading pediatricians and practitioners to refer cases of intussusception early. One has only to compare the durations of symptoms of series reported in the United States with those of Australia and England to realize what is yet to be attained in this

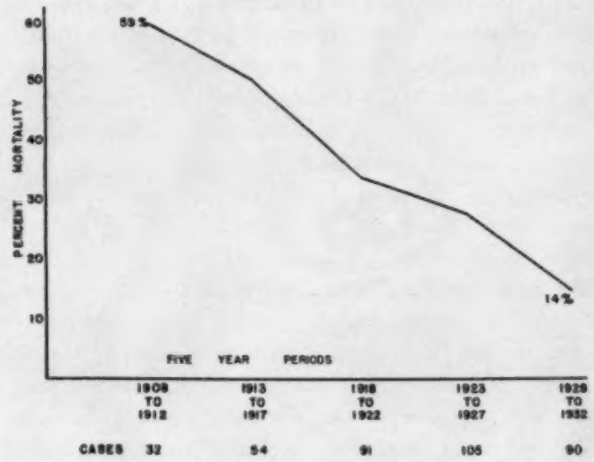

Fig. 6.—Mortality rates by five year periods, including all 372 cases.

country. Table 4 indicates the relation between the mortality in our series and the duration of symptoms, and figure 7 shows this relationship graphically.

Various authors have stated that if the children are seen within from twenty-four to forty-eight hours after the onset of symptoms the results are good. In our patients seen in the first thirty-six hours the mortality was 21 per cent for the first twenty-year period, whereas in the last five years we have had 60 such cases with no deaths.

Some of the reduction in mortality was unquestionably due to securing the cases earlier; formerly 52 per cent and recently 60 per cent were obtained in the first thirty-six hours. But improvement in the mortality rate has also been obtained by greater attention to postoperative care, for in table 4 it can be seen that in each of the time groupings (except one) there has been a reduction in the mortality in the second period as compared with the first.

Patients from private practice have always had a lower mortality than ward patients. In the first twenty year period there were 30 recoveries and 4 deaths, and in the last five years there were 10 recoveries and no deaths. In the private wing 80 per cent of the patients were seen within the first thirty-six hours—undoubtedly an important factor in decreasing the number of fatalities.

TABLE 4.—*Duration of Symptoms and Corresponding Mortality Statistics*

	1908-1927			1928-1932		
Duration of Symptoms	Living	Dead	Mortality, per Cent	Living	Dead	Mortality, per Cent
0 to 12 hours	55	4	7	35	0	0
12 to 24 hours	49	16	25	20	0	0
24 to 36 hours	12	11	49	5	0	0
36 to 48 hours	24	27	53	4	2	33
48 to 72 hours	15	18	53	3	2	40
72 to 96 hours	6	9	60	3	4	57
4 to 5 days	6	6	50	2	1	33
5 days and more	6	8	57	3	4	57
Time not stated	6	4	40	2	0	0
Totals	179	103	37	77	13	14

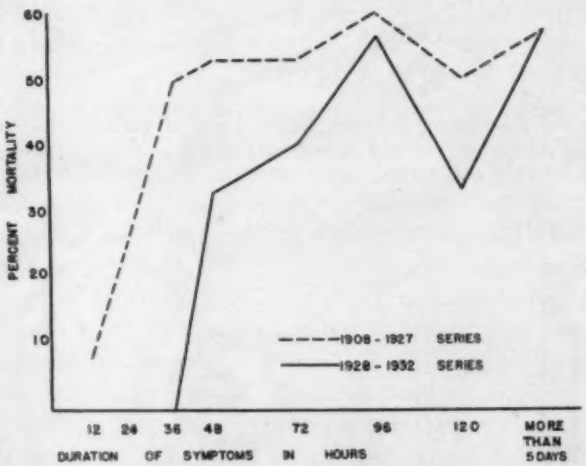

Fig. 7.—The relationship between the duration of symptoms and the corresponding mortality rates. The broken line represents the period from 1908 to 1927, and the solid line the period from 1928 to 1932.

In general, irrespective of the origin of the intussusception, the farther the mass progressed toward the anus, the higher was the related mortality (fig. 8). An exception to this rule has been those rare cases of colocolic type in which the mortality was somewhat lower owing to the fact that they gave early symptoms (rectal bleeding, etc.). This

increase in expectancy of death as the leading point approached the anus probably depended on increasing tension on the mesentery with resulting shock, vascular occlusions and greater difficulty in reduction.

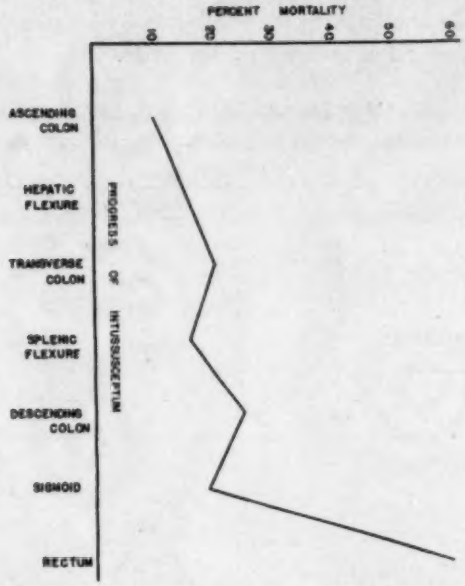

Fig. 8.—The relationship between the progress of the intussusceptum and the corresponding mortality rate, irrespective of the origin of the intussusception.

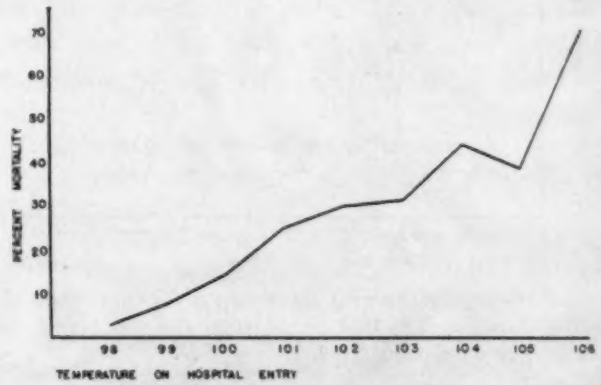

Fig. 9.—The relationship between the temperature on admission to the hospital and the corresponding expectancy of mortality.

The degrees of temperature had considerable prognostic value. Fever at the time of admission to the hospital was a bad sign, and with temperatures above 100 and 101 F. the expectancy of death rose rapidly. This is illustrated in figure 9. After operation practically all patients

had some fever for three or four days, which then subsided to normal temperature if there were no complications. A rise to 102 or 103 or even 104 F. was not unusual, but levels above 105 F. carried a grave and usually fatal prognosis.

PREOPERATIVE AND POSTOPERATIVE CARE

Everything possible was done to expedite operation. In the average cases no preoperative parenteral administration of fluid was practiced, but in the presence of marked dehydration dextrose was administered intravenously (10 cc. of 10 per cent solution of dextrose per pound of body weight) and saline solution subcutaneously (15 cc. of isotonic saline solution per pound of body weight). During operation a baby or young child was always wrapped with cotton batting to cover the arms, legs and chest completely. A hot water bottle was placed under the back to help prevent the loss of body heat. Atropine (without morphine) was given preoperatively, 1/1,000 grain (0.00006 Gm.) for patients under 1 year, 1/500 grain (0.00013 Gm.) for those between 1 and 2 years and correspondingly larger doses for older patients. Some English surgeons use heroic doses up to 1/150 grain (0.00043 Gm.) for infants, but we found no beneficial effect on the intestines from such doses, and hence employed the drug only for its action on the respiratory and salivary systems.

If no fluids had been administered before operation, they were immediately given as a routine when the child was returned to bed. The administration of fluids was repeated twice daily until dehydration was overcome and until adequate fluid was taken by mouth. Usually the parenteral administration of fluids was not repeated after the second postoperative day, but we have repeated it daily for from four to five days when indicated. By rectal tap 5 per cent dextrose was administered on return from the operating room and every four hours throughout the first postoperative day.

For the first postoperative day, or as long as there was vomiting, fluids without milk were offered every two or three hours. After vomiting had ceased, milk and whey were given, mixed in equal quantities, for an additional eighteen to twenty-four hours. Breast milk or a substitute was then given, but the full caloric or volume intake for the age and weight was not given until the fourth or fifth day. English surgeons offer the breast to suckling infants in from four to six hours after operation, but we do not like to give whole milk at such an early time, when there is danger of postanesthetic vomiting and aspiration.

Postoperative Complications.—Shock, dehydration and toxicity took the largest toll, and fully four fifths of those who died had these factors listed as the cause of death. Because such conditions caused most of

the fatalities, 85 per cent of the deaths occurred within forty-eight hours after entry into the hospital.

Peritonitis accounted for 6 deaths. This figure would probably have been higher had more autopsies been permitted. Bronchopneumonia was the cause of death in 5 patients, 2 of these having had advanced pneumonia at the time of entry into the hospital. Two patients had evisceration of the intestines when the wounds broke open on the tenth postoperative day. The wounds were resutured, but both patients succumbed one and two days later, respectively. Two other patients had poorly healing wounds, and because of impending evisceration the wounds were resutured successfully.

Not infrequently diarrhea developed during convalescence. This was probably due to secondary enteritis, and since the traumatized intestinal tract was more susceptible to infection, strict precautions had to be taken to guard against exposure to patients with dysentery. When such a complication developed, the oral intake was reduced, sedatives were given and fluids were administered parenterally.

SUBACUTE AND CHRONIC INTUSSUSCEPTION

Subacute intussusception has been defined as that in which the symptoms last for from five or six days to two weeks, and the chronic type as that in which the symptoms last for more than two weeks. In the first group there were 15 patients, 5 of whom lived and 10 of whom died. Only 1 had any demonstrable cause for the invagination (cecal polyp, recovery). In the chronic class 4 recovered and 1 died, and none had any demonstrable etiologic factor. In the two groups 3 patients were 3 years and 9 months, 6 years and 1 month and 9 years old, respectively, the remainder being 13 months old or younger. That these patients lived so long must have been due to the presence of incomplete intestinal obstruction and to the maintenance of the blood supply to the intussusceptum. Naturally, from only partial obstruction the symptoms were not so pronounced or so fulminating as those from acute intussusception, in which the bowel was usually completely occluded.

RECURRENT INTUSSUSCEPTION

In 1932 Thorndike reported 5 cases of recurrent intussuception from the Children's Hospital, Boston, and collected 75 more from the literature. He did not include the 9 cases of recurrent intussusception of Hipsley. Two other cases have been the subject of medical writings since then. With 2 additional cases which we have observed there have been at least 93 such cases.

In none of the 7 recurrent cases in our series was a mechanical cause found for the intussusception. No death has occurred in the recurrent cases. The time of recurrence varied from two months to three years after the initial attack. Six of the patients had one recurrence, and in each case only simple reduction was done. In one instance the appendix was also removed. The seventh patient had one recurrence for which reduction was performed, but following this there were three attacks suggestive of intussusception, in each of which there was apparently a spontaneous reduction. At exploration after the last attack no etiologic factor was found.

In the cases recorded in the literature the longest interval before recurrence was eight years and the shortest interval was thirty hours. The largest number of recurrences ever reported were in one of Hipsley's patients, who had six attacks after operative reduction.

Because of the relatively low incidence of recurrence, 1.8 per cent in our series, we believe that no time should be wasted at the primary operation in attempting procedures designed to prevent recurrence. A further reason for not undertaking any such operative procedure is the fact that a recurrence does not necessarily take place in the same location as the original intussusception. Thus, in Gray's case, with three attacks intussusception occurred in three different places. If there is any suspicion of an etiologic factor, such as a long mesentery, an abnormally mobile cecum, Meckel's diverticulum, a polyp, etc., it is better, if possible, to correct such abnormalities at a subsequent date when the patient is in better condition.

SUMMARY

Three hundred and seventy-two cases of intussusception are reported from the Children's Hospital, Boston.

Eighty-seven per cent of the patients were under 2 years of age, and 70 per cent were between the ages of 4 and 11 months. Sixty-one per cent were boys and 39 per cent were girls.

In only 5 per cent of the series were there demonstrable etiologic factors.

The important and most frequent symptoms were attacks of abdominal pain, pallor, sweating, vomiting and bloody stools occurring in a previously healthy child. The prominent physical findings were shock, dehydration, a palpable abdominal mass, blood from the rectum and possibly a mass palpable by rectal examination. Roentgen observations in the ileocolic variety were characteristic, but roentgen study was not necessary in the average case of acute intussusception.

The treatment was by operative reduction, and resection when reduction failed. Of 30 resections only 2 were successful. During the last five years, however, only 2 resections have been necessary in a series

of 90 cases. The mortality in all cases, in five year periods, has taken a continuous downward trend from 59 per cent in the 1908-1912 group to 14 per cent in the 1928-1932 group. In the last five years 60 cases were seen within thirty-six hours after the onset of symptoms and in all operation was performed without mortality.

It is believed that removal of a Meckel diverticulum or other cause of intussusception should be deferred if possible for a second operation.

Various factors and their relationship to the mortality are discussed. These include ranges of temperature, duration of symptoms, types of practice (private and charity) and location of the intussusception.

The preoperative and postoperative care are described.

Twenty cases of subacute and chronic intussusception are included, with a duration of symptoms varying from six days to eight weeks.

Seven cases of recurrent intussusception are included, an incidence of 1.8 per cent, without mortality.

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Lord, J. P.: Operation for Prevention of Recurrence of Intussusception, Tr. Western S. A., 1914, p. 111.

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INFLUENCE OF A LOCAL EXCESS OF CALCIUM AND PHOSPHORUS ON THE HEALING OF FRACTURES

AN EXPERIMENTAL STUDY

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As a result of recent advances in physiologic chemistry, many normal and pathologic processes are being considered from a chemical standpoint rather than anatomically or physiologically. Among these processes the formation of new bone in normal growth and in the repair of injury is receiving considerable attention. By certain writers, notably Leriche in France and Bancroft in this country, the process of ossification has been divorced from the influence of cells and is regarded as a purely chemical reaction which takes place extracellularly in the tissues around a fracture.

Accompanying this changing view is the tendency to explain nonunion on the basis of a general deficiency of calcium and phosphorus in the blood or a local deficiency of these elements at the site of the fracture. Hence some workers have attempted to influence the rate of healing of the bone by changing the concentration of calcium and phosphorus in the serum either by an alteration in the diet or by the administration of parathyroid extract-Collip; others have injected various salts of calcium and phosphorus at the site of fracture in the hope of accelerating the rate of repair.

That the calcification of rachitic bone in vitro depends on the character of the serum used or on the calcium and phosphorus content of an aqueous solution was shown by Shipley, Kramer and Howland.[1] They found that normal serum favored calcification, while rachitic serum did not permit it, and that calcification in an aqueous solution occurred most abundantly when the reaction and the content of calcium and phosphorus were those of normal serum. Further experimental and clinical evidence as to the importance of the concentration of calcium and

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This investigation was supported by funds from the Christine Breon Fund, the University of California.

1. Shipley, P. G.; Kramer, B., and Howland, J.: Studies upon Calcification in Vitro, Biochem. J. **20**:379, 1926.

phosphorus in the blood was provided by Peterson.[2] This author concluded from determinations of serum calcium and phosphorus in seventeen cases of nonunion and nine case of fracture which united normally that:

> No healing of the fracture takes place when the inorganic constituents, calcium and phosphorus, are so reduced that the product of these elements is less than thirty; little healing takes place between thirty and thirty-five; active healing results with a product between thirty-five and forty.

He drew similar conclusions from a study of fractures in dogs receiving normal diets and diets low in calcium and phosphorus.

Further clinical and experimental evidence was submitted by Tisdall and Harris,[3] who determined the serum calcium and phosphorus in normal human beings of all ages, in patients during the period of union of fractures and in dogs with fractures. These writers observed, "It is evident that a high concentration of phosphorus in the blood serum accompanies the deposition of bone salts during the periods of normal growth of bone and of repair of fractures." They further concluded:

> In the healing of fractures, two mechanisms are at work; one concerned with the maintaining of an adequate supply of bone salts in the blood, and the other with the taking up of these salts from the blood, and their precipitation in the tissue between the ends of the bone. Of these, the latter is apparently the more important process.

Other work has been reported which throws doubt on the significance of variations in the serum calcium and phosphorus in the healing of fractures. Henderson, Noble and Sandiford[4] determined the serum calcium and phosphorus in twenty clinical cases of ununited fracture which were compared with a series of cases in which there were no fractures. In both series the product of the values for serum calcium and serum phosphorus fell between 30 and 35. These authors stated: "It seems unlikely that bone formation is solely a question of physical chemistry. We are too imbued with the philosophy of Haldane to deny an important rôle to the bone forming cells themselves." An investigation of the effect of changes in the blood chemistry on the healing of experimental fractures in dogs was made by Ravdin and Morrison.[5] Normal dogs were compared with those in which the serum

2. Peterson, H. A.: A Clinical Study of Ununited Fractures with Special Reference to the Inorganic Bone-Forming Elements in the Blood Serum, J. Bone & Joint Surg. **6**:885, 1924.

3. Tisdall, F. F., and Harris, R. I.: Calcium and Phosphorus Metabolism in Patients with Fractures, J. A. M. A. **79**:884 (Sept. 9) 1922.

4. Henderson, M. S.; Noble, T. P., and Sandiford, K.: Ununited Fractures with Special Reference to the Chemistry of the Blood, J. Bone & Joint Surg. **8**:607, 1926.

5. Ravdin, I. S., and Morrison, M. E.; Ossification After Fracture, Arch. Surg. **17**:813 (Nov.) 1928.

calcium was raised by the administration of parathyroid extract or lowered by parathyroidectomy. These workers concluded, "We have not been able to prognosticate the rate of ossification after fracture from the calcium and phosphorus product, from the ion product or from the negative logarithm of the ion product."

A later study by Speed [6] along similar lines led to almost identical conclusions. This writer produced alterations in the blood calcium and phosphorus by changes in the diet of dogs and by parathyroidectomy. By this operation a decided delay in the healing of fractures was produced, but the dogs in which the serum calcium was raised or lowered by special diets showed normal healing.

Dragstedt and Kearns [7] reported experiments in which the repair of defects in the femurs of dogs was observed under three conditions, namely: (1) in normal dogs, (2) in dogs on which thyroparathyroidectomy had been performed and (3) in dogs to which parathyroid extract-Collip was given. They concluded that thyroparathyroidectomy delays the healing of a defect in the bone, although healing goes on at a normal rate if calcium is administered following this procedure. The administration of parathyroid extract-Collip in moderate amounts has little effect on the rate of healing, while large doses cause a definite impairment of healing.

In a study by Stocker [8] of the metabolism of minerals in fractures the patients with normal union showed a hypercalcemia and a normal content of phosphorus in the serum. Similar results were obtained in the patients with delayed union, although the hypercalcemia persisted for a longer period in the latter.

In the hope of influencing the rate of healing, many workers have injected various salts of calcium and phosphorus at the site of experimental fractures. Albee and Morrison [9] injected a suspension of tricalcium phosphate in a gap produced in the radius of a rabbit. The other radius, with a similar defect, served as a control. The average length of time required for union of the fracture treated with calcium phosphate was thirty-one days, as compared with the controls, which required an average of forty-two days.

6. Speed, K.: Blood Serum Calcium in Relation to the Healing of Fractures, J. Bone & Joint Surg. **13**:58, 1931.

7. Dragstedt, C. A., and Kearns, J. E., Jr.: Experimental Study of Bone Repair: Effect of Thyro-Parathyroidectomy and of the Administration of Parathormone, Arch. Surg. **24**:893 (June) 1932.

8. Stocker, H.: The Metabolism of Minerals and Its Relation to Internal Secretion in Fractures, Deutsche Ztschr. f. Chir. **231**:714, 1931.

9. Albee, F. H., and Morrison, H. F.: Studies in Bone Growth: Triple Calcium Phosphate as a Stimulus to Osteogenesis, Ann. Surg. **71**:32, 1920.

Eden [10] attempted to heal an operative gap in the radii of rabbits by filling the defect with calcium phosphate or carbonate, but this proved to be an unfavorable filling material, because it was too difficult to absorb. He obtained better results by filling the defect in the radius with a gelatin which contained calcium.

Cretin [11] found that the injection of the various mineral elements of bone between the ends of experimentally produced fractures resulted in a marked acceleration of the formation of callus and bone. Murray [12] carried out similar investigations in which he filled a gap of 2.5 cm. in a dog's radius with sterile powdered calcium carbonate and calcium phosphate, which was followed by solid bony union. The use of sterile powdered calcium hexose phosphate also proved successful, and union was even more rapid if fibrin from the dog's blood was placed in the gap before adding the calcium salt.

The experiments of Rollo [13] indicate that the injection of calcium glycerophosphate into the tissues around a fracture in rabbits serves to stimulate the formation of callus and bone. He found that this substance facilitated the closure of the gap in partial diaphyseal resection, while in controls the evolution of the callus was impeded by the interposed muscle.

A few surgeons have injected various salts of calcium and phosphorus into human beings in the hope of securing an acceleration of bone repair. Murray [14] used powdered calcium triple phosphate and calcium carbonate mixed with blood to fill the defect following saucerization of an infected compound fracture of the tibia. Cotton [15] injected salts of calcium and magnesium at the site of the fracture in a few clinical cases, but drew no conclusions from these trials. In addition to his previously described experimental work, Eden [10] injected secondary sodium phosphate at the site of the fracture in three instances of delayed healing in human beings. Consolidation resulted in all of the cases, two of which presented fractures of the femur and one a fracture of the tibia. The same author injected calcium glycerophosphate at the site of a bone graft of the femur with a good result.

In the injection of various substances at the site of fracture to stimulate ossification, the attempt has been made in most instances to

10. Eden, R.: Untersuchungen über Vorgange bei der Verknöckerung, Klin. Wchnschr. **2**:1798, 1923.

11. Cretin, A.: Etudes sur la calcification normale, Gaz. d. hôp. **97**:946, 1924.

12. Murray, C. R.: The Repair of Fractures, Minnesota Med. **13**:137, 1930.

13. Rollo, S.: Injection of Calcium Salts into Tissues Adjacent to Fractures under Pathologic Conditions, Ann. ital. di chir. **10**:1059, 1931.

14. Murray, C. R.: Delayed and Non-Union in Fractures in the Adult, Ann. Surg. **93**:961, 1931.

15. Cotton, F. J.: Dislocations and Joint Fractures, ed. 2, Philadelphia, W. B. Saunders Company, 1924, p. 39.

supply the elements which make up bone in their natural proportions. Some dispute exists as to the state in which calcium and phosphorus occur in bone. The orthophosphate of calcium, tricalcium phosphate or $Ca_3(PO_4)_2$ is given by most textbooks as the formula for bone (Roscoe and Schorlemmer [16]). According to Bogert and Hastings [17] the composition of bone can be represented by the formula $CaCO_3.n\ Ca_3(PO_4)_2$, in which n is approximately 2 in untreated bone. Quantitative determinations of calcium and phosphorus in powdered bone (Shear and Kramer [18]) indicate that the probable formula for bone salts is $CaHPO_4$, the dicalcium phosphate. As has been noted previously, the salts injected at the site of fractures include tricalcium phosphate, calcium glycerophosphate, calcium hexose phosphate, calcium carbonate, calcium in gelatin and secondary sodium phosphate (Na_2HPO_4). In the present study use has been made of the three calcium phosphates (tricalcium, dicalcium and monocalcium) and of calcium glycerophosphate.

METHODS

An operative defect, between 0.5 and 1 cm. in length, was made in the radii of seventeen rabbits. One side served as a control, while the defect in the opposite radius was filled with a dry, powdered salt of calcium and phosphorus. In a few cases, a suspension of the salt was injected at the site of the fracture a few days after the segment of radius was excised. The rate and extent of the callus formation were observed in roentgenograms taken at weekly intervals following the operations. The animals were killed from three to ten weeks after operation, and a microscopic examination of each radius was made.

The following salts of calcium and phophorus were used:

Monocalcium phosphate	$Ca(H_2PO_4)_2$	4 experiments (17, 18, 20, 22)
Tricalcium phosphate	$Ca_3(PO_4)_2$	6 experiments (71, 72, 73, 74, 75, 76)
Dicalcium phosphate	$CaHPO_4$	2 experiments (77, 78)
Calcium glycerophosphate		5 experiments (81, 82, 83, 84, 85)

RESULTS

The results obtained from these experiments are best considered under four headings, depending on the salt which was used.

Monocalcium Phosphate.—In rabbit 17 both defects became filled with new bone, although union was somewhat delayed on the side in which the defect was filled with monocalcium phosphate. In experiment 20 the defect in the left radius was filled with the salt at the time of operation, while the defect in the right radius served as a control.

16. Roscoe, H. E., and Schorlemmer, C.: Treatise on Chemistry, New York, The Macmillan Company, 1913, vol. 2, p. 557.

17. Bogert, L. J., and Hastings, A. B.: Calcium Salts of Bone, J. Biol. Chem. 94:473 (Dec.) 1931.

18. Shear, M. J., and Kramer, B.: Composition of Bone, J. Biol. Chem. 79:105, 1928.

The animal died twenty-three days later, at which time there was an extensive abscess in the left foreleg, and the muscles appeared necrotic. Roentgenograms (fig. 1) showed that the gap in the right radius was partially filled with callus, while no closure of the defect was seen in the left radius. Microscopic sections through the two defects (fig. 2) revealed an abscess at the site of the defect in the left radius, while the gap in the opposite radius was filled with cartilage and early callus. In experiment 18 the defects were filled with bone chips on the right side and with monocalcium phosphate on the left. Union occurred in the former after twenty-one days and on the side containing the salt only after forty-two days. In the other case in which the salt was used, the rabbit (22) died on the third day with no evidence of healing in either radius.

Tricalcium Phosphate.—The results in the six experiments in which tricalcium phosphate was placed in the defect of one radius fall into two equal groups: In the first, which consisted of experiments 71, 72 and 73, both radii healed in approximately the same length of time. The second group, which consisted of experiments 74, 75 and 76, showed complete although delayed healing of the defect in the radius in which tricalcium phosphate had been placed, while the other defect, containing no salt, failed to close. There was no variation in the methods employed in these six experiments to account for the difference in results. As an example of the first group, experiment 72 showed an equal rate of callus formation on the two sides, as revealed by roentgenograms (fig. 3), and in microscopic sections (fig. 4) both radii presented the same appearance. In the second group, roentgenograms (fig. 5) in experiment 76 showed a complete closure of the defect containing tricalcium phosphate, while typical nonunion occurred in the opposite radius. Microscopic sections (fig. 6) substantiated the conclusions drawn from the roentgenograms.

Dicalcium Phosphate.—The dicalcium phosphate was employed in two instances, in both of which union occurred in both radii at approximately the same time. In one of these experiments (78), roentgenograms (fig. 7) showed that the defect in each radius was fairly well filled after three weeks and firmly united after six weeks. In microscopic pictures (fig. 8) the same appearance of complete restoration of the cortex was seen in both radii.

Calcium Glycerophosphate.—This salt was used in five rabbits, two of which died in less than one week. In the three rabbits which lived until union occurred, the slight difference in the rate of healing favored the side in which no salt was placed. Figure 9 shows the rate of healing as indicated roentgenologically, and figure 10 presents an almost identical appearance of the two radii eight weeks after operation (experiment 82).

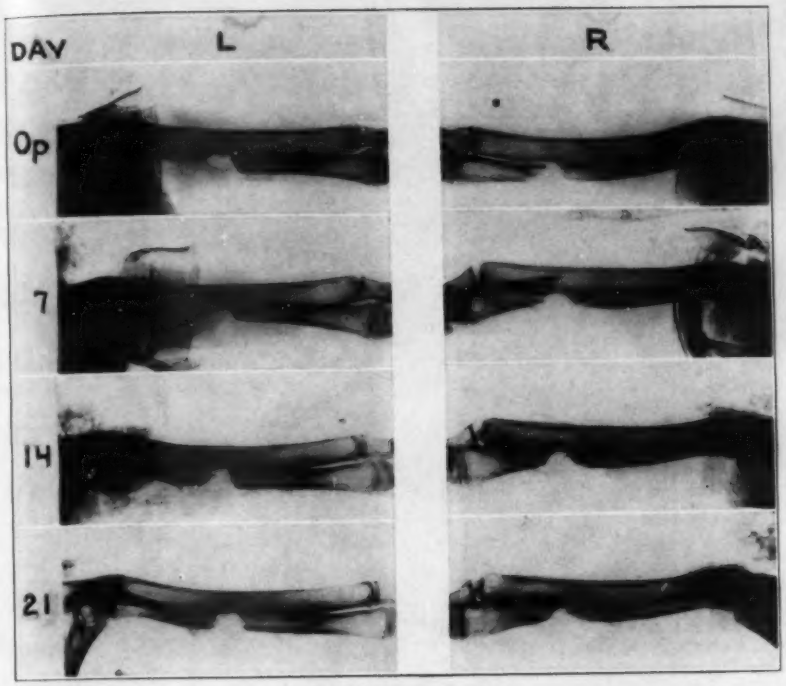

Fig. 1.—Roentgenograms in experiment 20.

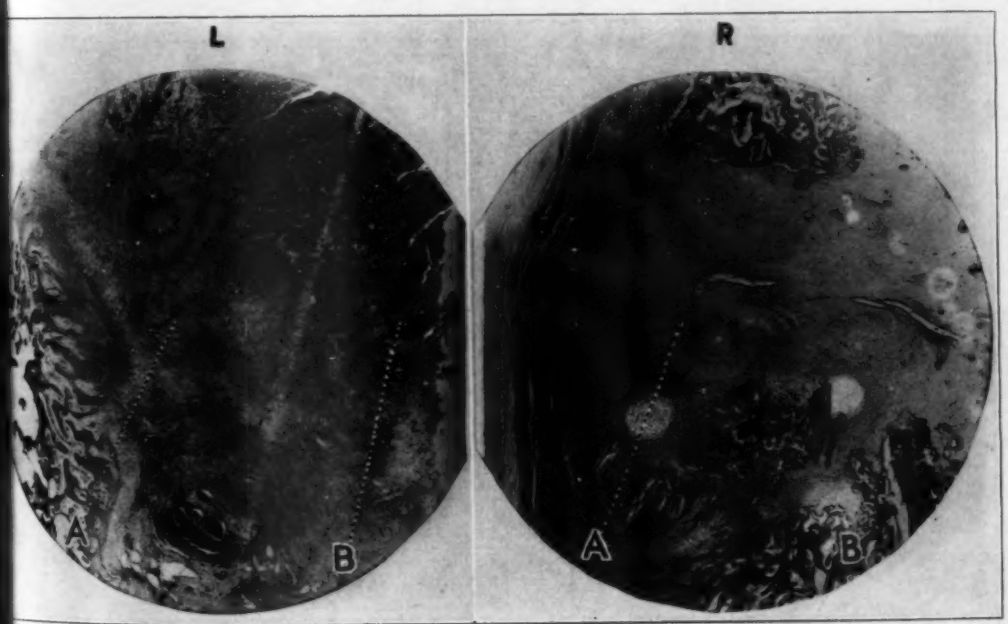

Fig. 2.—Photomicrographs of fracture site in experiment 20. In the section of the left radius (*L*), *A* indicates necrotic muscle and *B* an abscess; in the section of the right radius (*R*), *A* indicates cartilage and *B* old cortex.

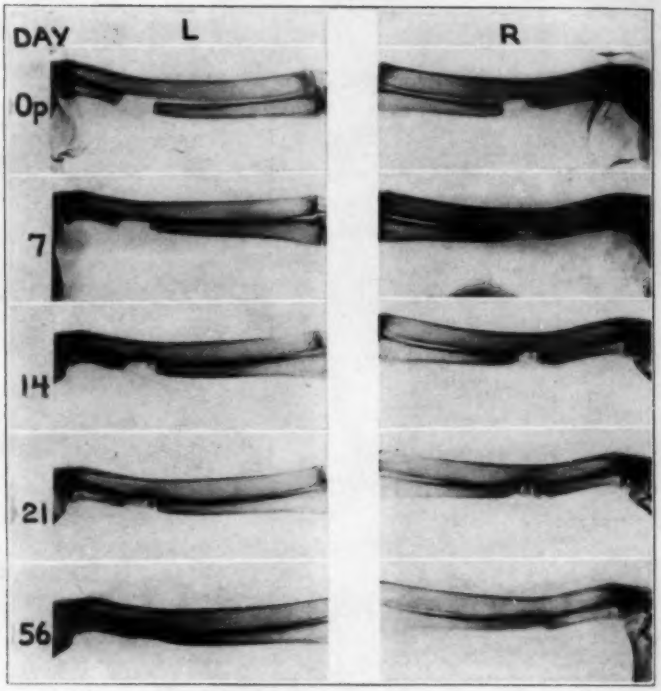

Fig. 3.—Roentgenograms in experiment 72.

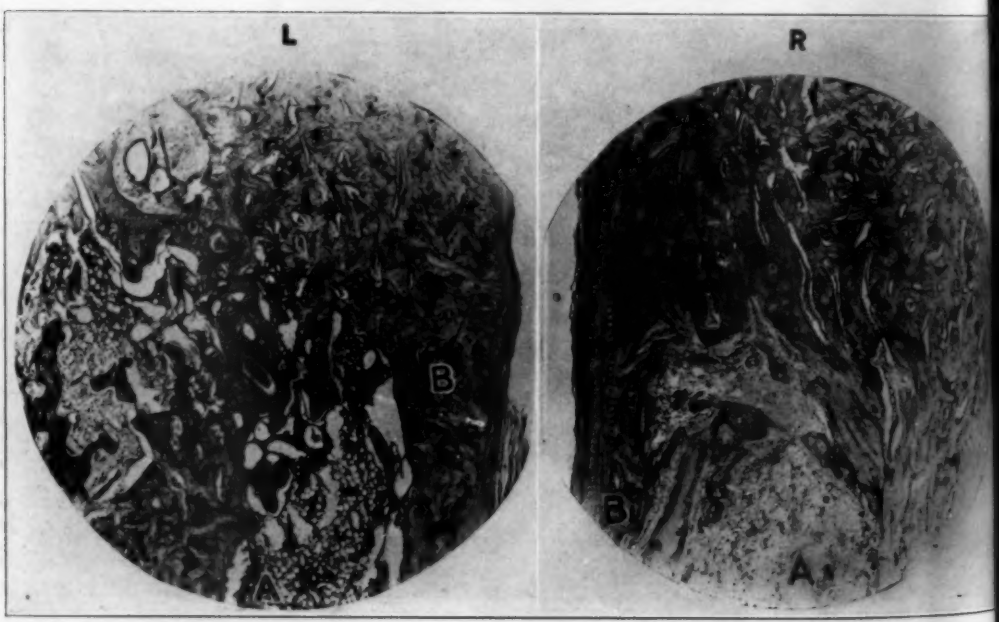

Fig. 4.—Photomicrographs of the site of fracture in experiment 72. *A* indicates marrow and *B* new cortex.

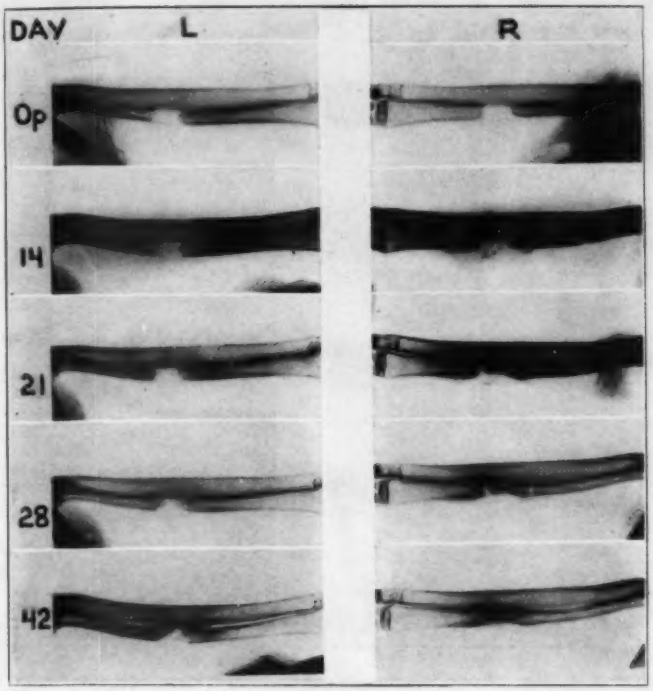

Fig. 5.—Roentgenograms in experiment 76.

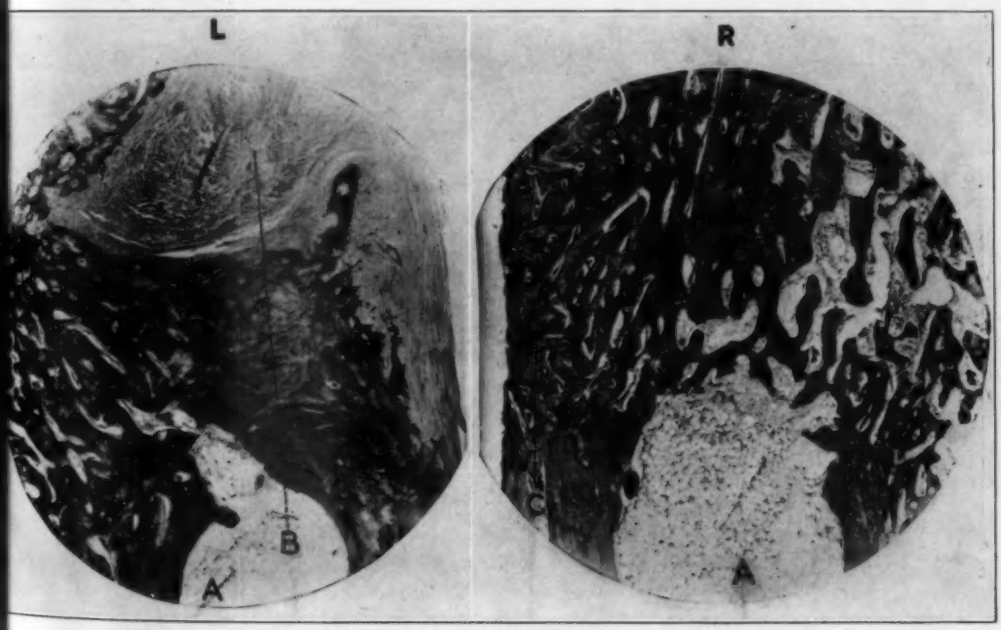

Fig. 6.—Photomicrographs of the site of fracture in experiment 76. *A* indicates marrow; *B*, the defect; *C*, cortex.

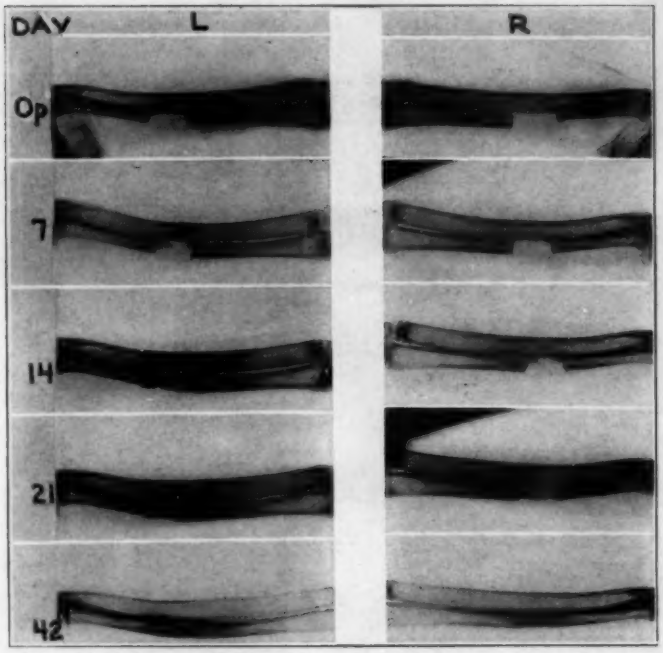

Fig. 7.—Roentgenograms in experiment 78.

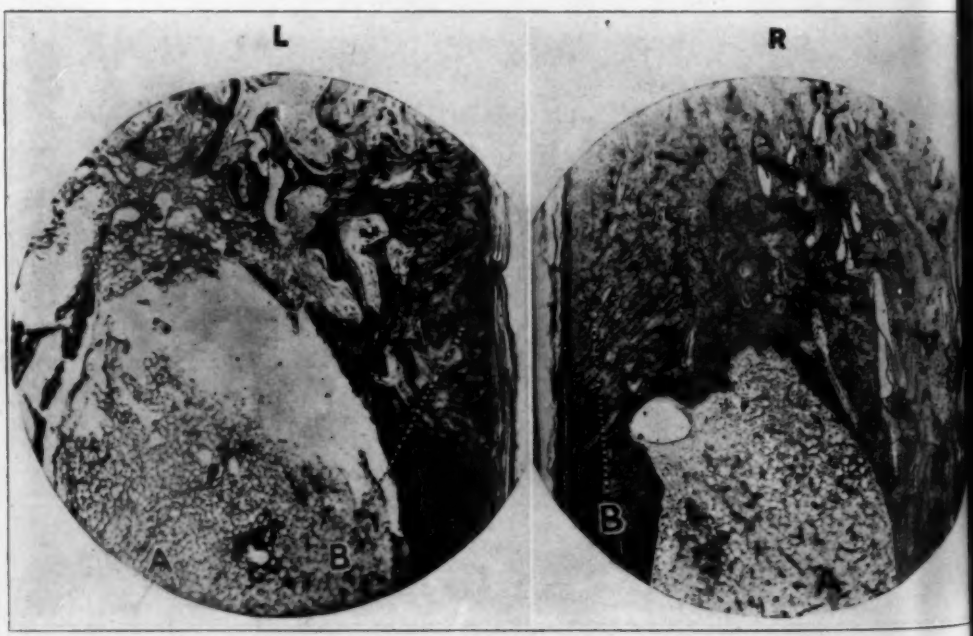

Fig. 8.—Photomicrographs of the site of fracture in experiment 78. *A* indicates marrow and *B* new cortex.

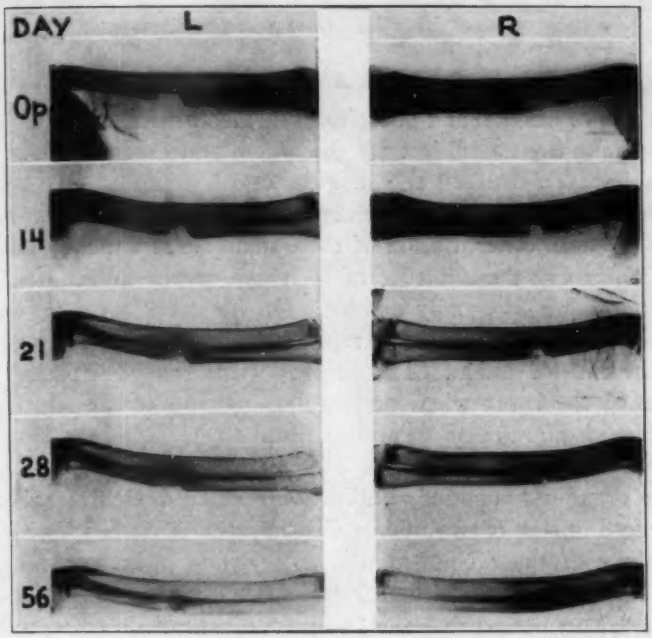

Fig. 9.—Roentgenograms in experiment 82.

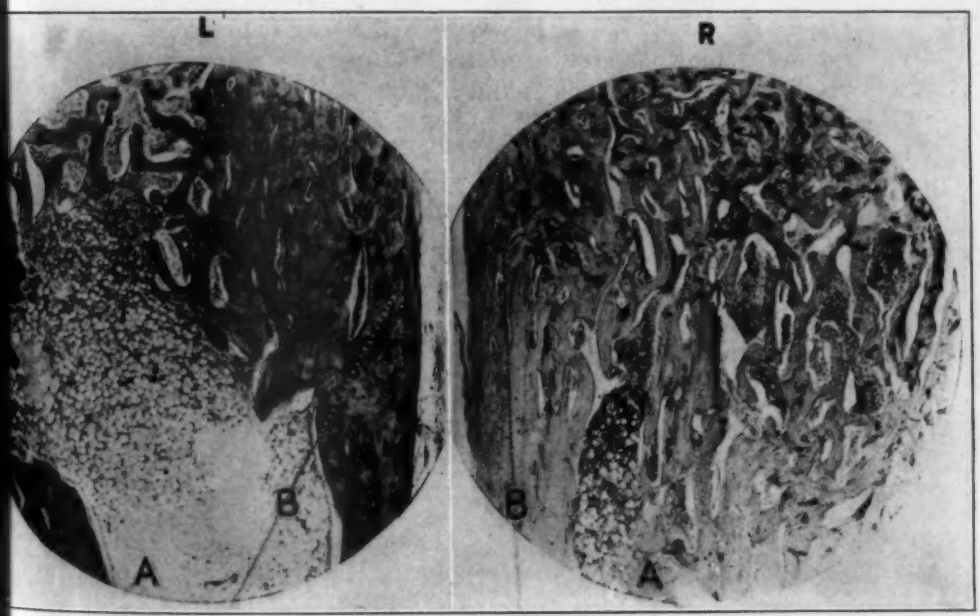

Fig. 10.—Photomicrographs of the site of fracture in experiment 82. *A* indicates marrow and *B* new cortex.

SUMMARY

The rôle of calcium and phosphorus metabolism in the healing of fractures has long been a subject for discussion and investigation. Certain workers have emphasized the importance of calcium and phosphorus as found in the blood serum, while others have turned their attention more to the local concentration of these minerals at the site of the fracture. Concerning the influence of increased serum values, opinion and evidence seem about equally divided. On the other hand, an excess of the local supply of these salts is reported almost unanimously as accelerating the rate of union. The present work has been limited to the influence of the latter when present throughout the period of healing of a defect in the radii of apparently normal rabbits.

After the use of three forms of inorganic calcium and phosphorus and one organic compound, healing was delayed in five rabbits and uninfluenced in seven; two rabbits died in the first week after operation, and in three of the rabbits in which tricalcium phosphate was added, the healing was delayed on both sides, although complete union eventually resulted on the treated side, while the control defects went on to typical nonunion. The reason for this delay is not apparent. However, the conclusion seems justified that in certain cases of delayed union tricalcium phosphate is an aid to union.

None of the calcium and phosphorus compounds used in excess seemed capable of accelerating the normal rate of healing. In this respect the results fail to follow the well recognized chemical law that increasing the concentration of the reacting substances speeds up the reaction. Because of this fact, it is probable that the process of ossification is more than the purely chemical equation which certain writers describe.

CONCLUSIONS

1. In normal healing under favorable conditions the continued presence of an excess of calcium and phosphorus at the site of fracture either did not influence the rate of union or retarded it.

2. In delayed healing resulting from unknown causes the presence of tricalcium phosphate at the site of the fracture appeared to favor the union.

3. In no case did the presence of monocalcium phosphate, dicalcium phosphate or calcium glycerophosphate have a favorable influence.

COMPARATIVE VALUE OF INTRAVENOUS SCLEROSING SUBSTANCES

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AND
HOWARD MAHORNER, M.D.
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In a previous communication, Garside and one of us (A. O.)[1] reported the results of studies on the effect of the intravenous injection of certain sclerosing solutions. The present paper is in reality a report of the continuation of that work, comprising a similar study of nine additional solutions. The twenty solutions in the first study and the nine in the present study include practically all the important drugs advocated for use in the treatment of varicose veins by injection and in addition certain new drugs that have not been used before for this purpose, either experimentally or clinically. Comparison of the results shows the relative value of the solutions in their potency as thrombosing agents producing changes in the walls of the veins.

The solutions used in this investigation were 10 and 5 per cent solutions of sodium morrhuate (our own); 5, 3 and 2 per cent solutions of sodium gynocardate; 5, 3 and 2 per cent solutions of sodium hydnocarpate, and a 5 per cent solution of sodium morrhuate (Searle). Our own sodium morrhuate was prepared in the chemical laboratory of the department of surgery. The solutions of sodium gynocardate, sodium hydnocarpate and our own sodium morrhuate were dissolved in physiologic solution of sodium chloride. Searle's sodium morrhuate is prepared in benzyl alcohol.

Sodium morrhuate is obtained from cod liver oil, whereas sodium gynocardate is prepared from chaulmoogra oil, and sodium hydnocarpate from an oil closely resembling chaulmoogra oil, obtained from the seed of a tropical tree, Hydnocarpus wightiana.[2]

METHOD

The method of study was that used by Garside and one of us (A. O.).[1] Dogs were selected as the test animals. Veins in each of the four legs were used.

From the Department of Surgery, Tulane University School of Medicine.

1. Ochsner, Alton, and Garside, Earl: The Intravenous Injection of Sclerosing Substances, Ann. Surg. **96**:691, 1932.

2. Sodium gynocardate and sodium hydnocarpate were used because of a suggestion made by Sir Leonard Rogers (Intravenous Sclerosing Injections, Brit. M. J. **2**:120, 1930).

In the hindlegs, four injections were made into the long saphenous veins. The levels of injection were: (1) at the dorsum of the foot, (2) at the ankle, (3) at the middle third of the leg and (4) at the level of the knee. In the forelegs injections were made into the antebrachial cephalic veins[3] (1) at the level of the paw, (2) at the level of the wrist, (3) at the middle third of the foreleg and (4) at the level of the elbow joint. Thus, in each dog there were sixteen injections, four in each leg, but only one drug was used in any one leg, though it was injected at four different levels. Generally a different solution was used for each leg. After the injection was completed, a ring was marked around the area of injection with a moistened silver nitrate stick. This method of marking was satisfactory, and it enabled us subsequently to remove with accuracy the vein into which injection was made at the level of the injection.

Each drug was injected sixteen times, so for each drug sixteen portions of vein were subsequently removed, representing different periods of time elapsed after the injection of the drug. The time intervals at which portions were removed after the injection of each solution were: one-half hour, one, three, six, twelve, twenty-four and forty-eight hours; three, four, six, ten, fourteen and twenty-one days, and four, six and eight weeks.

In removing the vein sections the area encircled by the silver nitrate mark was infiltrated subcutaneously with procaine hydrochloride. A longitudinal incision about 2 cm. in length was made over the course of the vein, the vein was identified, and the surrounding tissues, including the nerve, were carefully dissected free from it, caution being taken not to dislodge a thrombus from the lumen of the vein. The vein was clamped at each end of a segment (proximal end first) about 1 cm. in length, and the intervening segment was removed. The vein was then ligated proximal and distal to the clamps, and the wound was closed with silk. In removing the sections, the more distal one was always removed first and then in succession the more proximal segments. It was presumed that removal of the segments at different times would not dispose to thrombosis by interfering with the return of blood, even if we must admit the slight possibility that removal of some *vis a tergo* might result in propagation of a thrombus to the next higher level. The belief that thrombosis at the next higher level did not occur because of this was supported by the fact that invariably the longer "intervaled" sections showed lower percentages of thromboses than did the earlier sections; and one would have expected the opposite, had the theoretical reason been an actual fact. Moreover, the findings in veins showing changes were quite constant for the different periods. We believe that we can explain this lower percentage of thrombosis after the longer periods by reasons other than inaccuracies.

The veins were prepared for microscopic study by cutting cross-sections and staining them with hematoxylin and eosin and Mallory's connective tissue stain, and in some instances with Verhoeff's elastic tissue stain.

In studying the sections microscopically, the results were recorded in four grades representing different degrees of change: from 0 to 25 per cent, grade I; from 25 to 50 per cent, grade II; from 50 to 75 per cent, grade III, and from

3. Ellenberger, W., and Baum, H.: Anatomie des Hundes, Berlin, Paul Parey, 1891.

75 to 100 per cent, grade IV. The observations were divided in the following manner:

1. The lumen
   (*a*) Thrombosis
2. The intima
   (*a*) Endothelial destruction
   (*b*) Exposure of nuclei
   (*c*) Vacuolation of cells
   (*d*) Pyknosis
3. The internal elastic lamina (whether it was intact or had been completely or partially destroyed)
4. The media
   (*a*) Edema
   (*b*) Leukocytic infiltration
   (*c*) Hemorrhage
   (*d*) Connective tissue proliferation
   (*e*) Presence of new blood vessels
   (*f*) Hyaline degeneration and coagulation necrosis of the muscle
   (*g*) Atrophy of the muscle
5. The adventitia
   (*a*) Edema
   (*b*) Hemorrhage
   (*c*) Presence of new blood vessels
   (*d*) Leukocytic infiltration
   (*e*) Hyperemia
   (*f*) Connective tissue proliferation

The grades I to IV of the thrombus indicate whether the thrombus completely occluded the lumen (grade IV), as it generally did if it was present, or whether it only partially occluded the lumen. Moreover, the grade of organization was studied in each thrombus. When the organization was just beginning, it was graded I. When the connective tissue cells had advanced halfway to the center of the clot, organization was graded II. When the connective tissue cells had advanced to the center but recanalization did not seem to be complete, it was graded III, and when fibrosis and recanalization seemed to be complete, it was graded IV.

Endothelial destruction was graded on the percentage of the endothelial cells that had completely disappeared. The two most important criteria as to the sclerosing value of the various substances were the presence of a thrombus and the destruction of endothelial cells.

The grading of the other changes is in each instance an individual evaluation of the percentage of the change occurring. Such a method is not strictly mathematically accurate and has an associated percentage of error. However, as one of us (A. O.) had also studied the slides in a previous analogous study [1] of twenty sclerosing substances, the results in the two investigations are comparable, and it is possible to indicate the most effective of the twenty-nine solutions.

CHANGES IN THE INTIMA

Some sclerosing substances injure the cell by dehydration, e. g., hypertonic salt and sugar solutions; others, by direct chemical injury.

We have observed these changes in fixed subcutaneous tissue in another study of the action of sclerosing substances on tissues and will report the results in a subsequent paper. When the intimal cells are sufficiently injured, they become detached and are carried away by the blood stream. It is destruction of the intima which results in the precipitation of a thrombus. Sclerosing substances do not hasten the coagulation time of the blood. We have proved this with adequate control in vitro by the addition of 0.5 cc. of quinine and urea hydrochloride to 1 cc. of freshly drawn blood. The coagulation time was not reduced, but slightly lengthened. The same result was obtained with Searle's sodium morrhuate.

Pyknosis.—One of the earliest appearances that may give evidence of a retrogressive change in the cell is a more densely staining nucleus. Slight grades of such a change are difficult to distinguish from the normal appearance of the cell, and it is probable that fixing and staining my produce some of the changes which appear to be pyknosis, karyolysis or karyorrhexis. In some instances we observed pyknosis in a vessel which otherwise appeared to be normal and in sections removed at long intervals after the injection of sclerosing substances. Such a change would throw some doubt on the value of a darkly stained small nucleus as a sign of injury by the sclerosing solution. It possibly indicates that the changes we record as pyknosis occurred after the vessel had been removed from the animal. Sometimes the higher percentages of pyknosis occurred in the series of veins into which drugs were injected which caused the lowest percentage of endothelial destruction and thrombosis. Sodium hydnocarpate, 2 per cent, showed 44 per cent pyknosis and 12.5 per cent thrombosis, whereas 5 per cent sodium gynocardate showed an average of 25 per cent pyknosis with 50 per cent thrombosis. This is explained by the fact that when thrombosis occurs the intima is partially or completely absent, and thus in the averaging of results instead of there being sixteen veins to show pyknosis there are in reality fewer.

Vacuolation.—This change (fig. 1) appears to be an intracellular edema and was irregular and inconstant. It was present in some sections of veins which had been treated with practically every one of the nine solutions under consideration. Its significance, like pyknosis, is difficult to interpret, and comparison of the average vacuolation occurring from the different agents leaves no clue as to the meaning. It is not necessarily an early change, as with our own sodium morrhuate solution vacuolation did not occur in the sections removed one-half hour or six hours after injection (sections removed one and three hours after injection showed marked endothelial destruction), but it did occur in the sections removed forty-eight hours, three days and fourteen days after

injection, being absent in all others. Such irregularities in the occurrence of vacuolation may be found in the results of almost any of the sclerosing agents.

Exposure of Nuclei.—By this change we mean that the cytoplasm on the free side of the endothelial cells lining the lumen of a vessel had been apparently completely destroyed or in some way removed so that

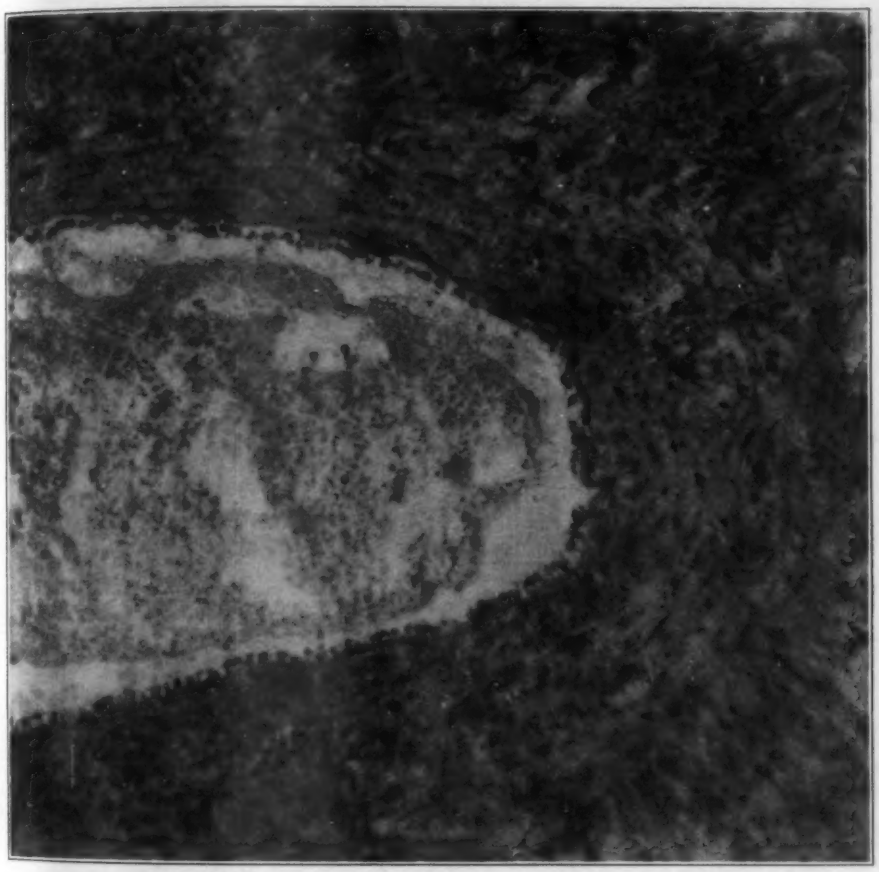

Fig. 1.—Photomicrograph of a vein showing vacuolation of cells of the intima forty-eight hours after the injection of 2 per cent sodium gynocardate.

the nucleus seemed to lie immediately under the cell membrane. Such a change was inversely proportional to the incidence of complete destruction of the endothelium. It was observed in some sections even when there were no other changes throughout the section, and it is not regarded as a reliable sign of injury resulting from the sclerosing substances.

Thrombosis and Endothelial Destruction.—Thrombosis did not occur in any instance in which there was no destruction of the endothelium.

Liberation of thrombokinase seems essential for precipitation of the thrombus. A graphic representation of the degree and incidence of thrombosis is shown in figure 2. A thrombus was present in 71 per cent of the sections of veins into which Searle's sodium morrhuate was injected, and endothelial destruction was present in the same percentage. Some endothelial destruction was present in 75 per cent of the sections of veins treated with 5 per cent sodium gynocardate, but thrombosis was present in only 50 per cent. However, endothelial destruction was graded IV in only 25 per cent of the sections treated with 5 per cent sodium gynocardate, whereas it was graded IV in 71 per cent of the sections treated with Searle's sodium morrhuate (figs. 2 and 3). Thus,

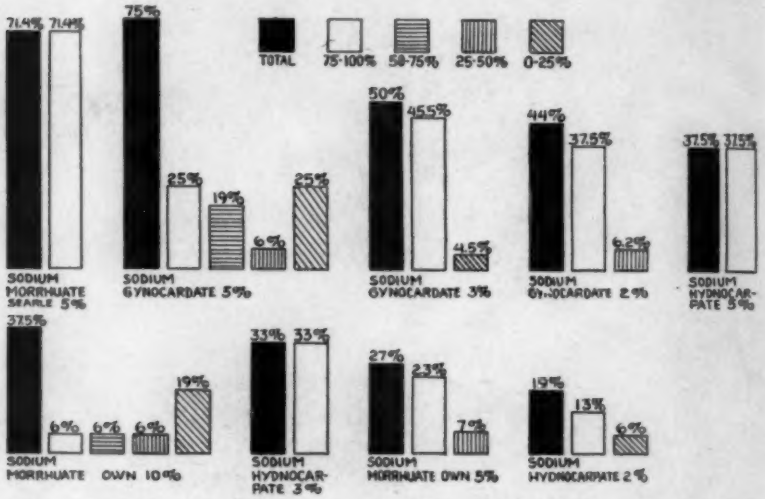

Fig. 2.—Graphic representation of the incidence and degree of endothelial destruction after intravenous injection of nine different sclerosing solutions. Four grades of destruction are indicated. Black represents the total destruction for each substance.

it would appear that experimentally Searle's sodium morrhuate is more effective than 5 per cent sodium gynocardate in producing destruction of the endothelium and thrombosis when injected into a vein. In their effectiveness in production of thrombosis the nine drugs used by us may be arranged as in figure 2. The effectiveness of the various solutions in producing thrombosis is as follows: Searle's sodium morrhuate, 71.4 per cent thrombosis; 5 per cent sodium gynocardate, 50 per cent; 3 per cent sodium gynocardate, 50 per cent; 2 per cent sodium gynocardate, 44 per cent; 5 per cent hydnocarpate, 37.5 per cent; 5 per cent sodium morrhuate (our own), 33 per cent; 3 per cent sodium hydnocarpate, 33 per cent; 10 per cent (our own), sodium morrhuate, 19 per cent; 2 per cent sodium hydnocarpate, 12.5 per cent (fig. 4). The discrep-

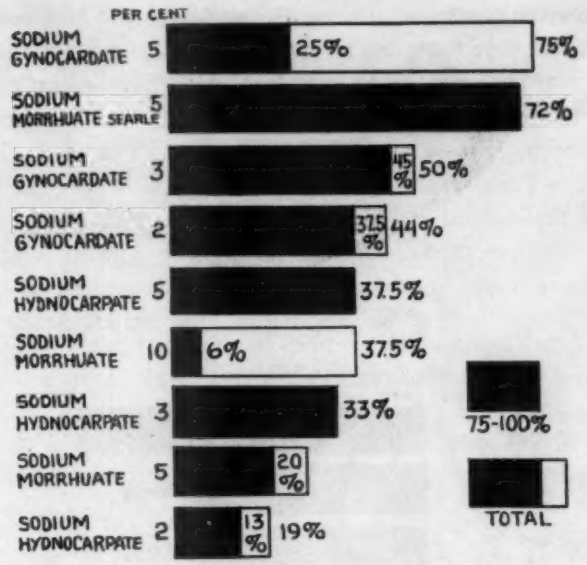

Fig. 3.—Graphic representation of comparative endothelial destruction produced by intravenous injection of sclerosing solutions. Black represents grade IV destruction of endothelium; the whole block, the total incidence of destruction of any grade whatsoever.

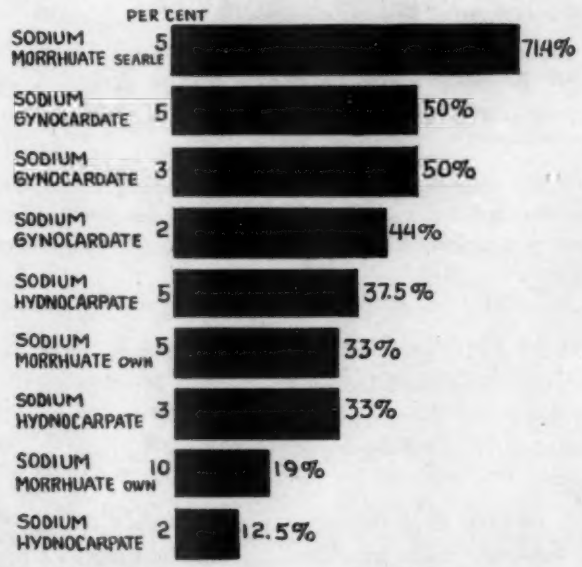

Fig. 4.—Graphic representation of relative thrombus-producing effectiveness of nine different sclerosing solutions.

ancy between the results obtained with our own 5 per cent sodium morrhuate (33 per cent thrombosis) and with Searle's 5 per cent sodium morrhuate may be due to the fact that in preparing our product we dissolved the sodium morrhuate in physiologic solution of sodium chloride, whereas Searle's sodium morrhuate is prepared with benzyl alcohol. It is possible that the benzyl alcohol enhances the sclerosing property of the sodium morrhuate. This is being investigated further.

When the three most effective thrombus-producing drugs in the study of Garside and one of us (A. O.)[1] are compared with those in the present series, three solutions in the latter series, Searle's sodium

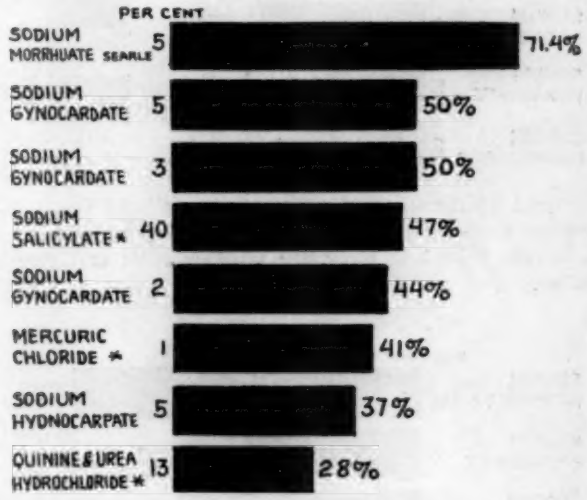

Fig. 5.—Graphic representation of thrombus-producing effectiveness of eight intravenous sclerosing solutions selected from nine solutions studied by us and twenty studied by Garside and one of us (A. O.). Three solutions from the latter study are marked X.

morrhuate and 5 and 3 per cent sodium gynocardate, were more potent in producing thrombus than the most effective solution (sodium salicylate, 40 per cent) in the former series (fig. 5). Quinine and urea hydrochloride was only ninth in thrombus-producing effectiveness in the entire series.

We are somewhat at a loss to explain the fact that in practically all instances we found more thrombosis in the eight sections representing early periods after injection, i. e., from one-half hour to three days, than in the eight sections representing longer periods, i. e., from four days

to eight weeks. When the periods are thus separated into two groups, the following percentages were found for our four most effective drugs:

	Thrombosis in Sections	
	1st period	2d period
Searle's sodium morrhuate, 5 per cent.....	50	21.5
Sodium gynocardate, 5 per cent.....	31	19.0
Sodium gynocardate, 3 per cent.....	25	25.0
Sodium gynocardate, 2 per cent.....	25	19.0

This discrepancy is hard to explain. It is possible that in the process of repair a clot might not go on to complete fibrosis and organization, but that blood circulating apparently through an old clot, as has been described by one of us (H. M.),[4] might gradually remove the thrombus. Such a process does not seem probable in our present knowledge of thrombosis, but there are appearances in clots that are highly suggestive that this does occur.

Organization.—Organization of a thrombus in a vessel occurs according to a definite process which has been adequately described by numerous pathologists. In this study organization begins shortly after the thrombus is precipitated. Very definite evidence of the ingress of fibroblasts into the periphery of a thrombus is present after forty-eight hours (fig. 6). On the other hand, there was no evidence of organization in one section removed six days after injection. In this vein propagation of a thrombus probably occurred, and the section was cut across the last precipitated area. Organization with recanalization seems to be complete by the tenth to the fourteenth day (figs. 7 and 8).

DESTRUCTION OF THE INTERNAL ELASTIC LAMINA

Definite evidence of destruction of the internal elastic lamina was observed in some of the sections. In some instances it was simply raised out of position and projected into the lumen. In other instances it was fragmented; in still other sections it was completely absent (fig. 9). The normal elastic lamina was always intact when the endothelium had not been destroyed. Whenever there had been destruction of the lamina there was a clot in the lumen. However, the reverse was not true, viz., that destruction of the internal elastic lamina was always present when a clot was found. Searle's sodium morrhuate produced some injury to the lamina in the highest percentage of instances (35.6 per cent). Both 3 per cent sodium gynocardate and 5 per cent sodium hydnocarpate pro-

4. Brown, G.; Allen, E. V., and Mahorner, H. R.: Thrombo-Angiitis Obliterans, Philadelphia, W. B. Saunders Company, 1928.

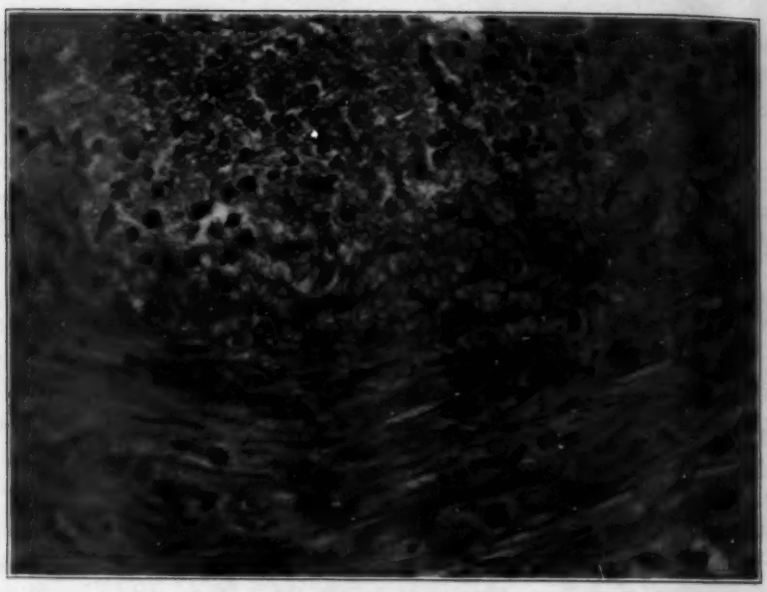

Fig. 6.—Photomicrograph of a vein showing the ingress of fibroblasts in a clot forty-eight hours after the intravenous injection of 3 per cent sodium gynocardate.

Fig. 7.—Photomicrograph of a vein showing different degrees of organization in the same lumen; one part is a secondary thrombus. The section was removed ten days after the injection of Searle's sodium morrhuate.

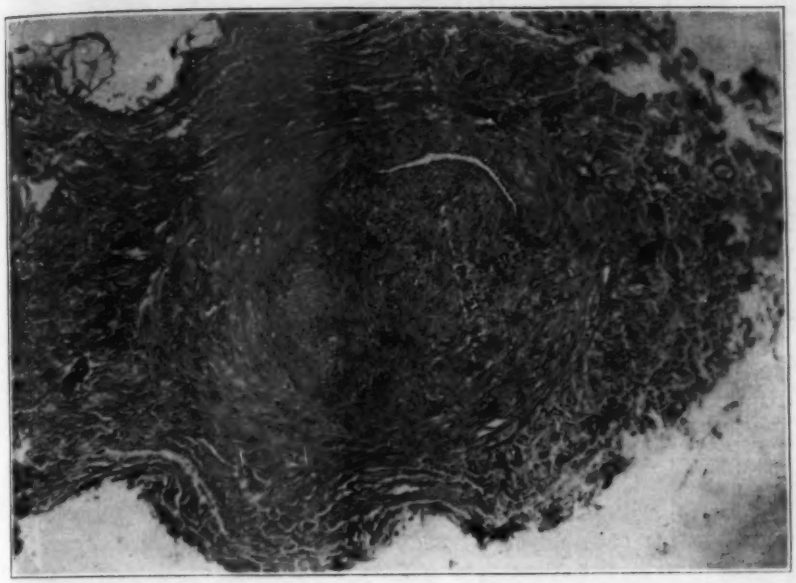

Fig. 8.—Photomicrograph of a vein showing organization of a thrombus practically complete fourteen days after the intravenous injection of 3 per cent sodium gynocardate.

Fig. 9.—Photomicrograph of a vein showing coagulation necrosis of the media, destruction of the intima and internal elastic lamina twenty-four hours after the injection of Searle's sodium morrhuate.

TABLE 1.—*Degree and Incidence of Changes in Lumen, Intima and Internal Elastic Lamina After Intravenous Injection of Nine Different Sclerosing Solutions*

	Destruction					Vacuolation					Exposure of Nuclei					Thrombosis					Total Injury	Pro-liferation	Pyknosis	Internal Elastic Lamina Destroyed				
	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%				Total	0-25%	25-50%	50-75%	75-100%
Sodium morrhuate, 5% (Searle's)	71.4	0	0	0	71.4	7.1	7.1	0	0	0	28.0	7.0	21.0	0	0	71.4	0	0	0	71.4	100.0	7.1	0	35.6	0	14.2	0	21.3
Sodium gynocardate, 5%	75.0	25.0	6.25	18.8	25.0	12.5	6.0	0	6.0	0	56.3	18.8	25.0	12.5	0	50.0	0	6.2	0	43.8	87.5	12.5	25.0	18.8	0	6.0	0	12.5
Sodium gynocardate, 3%	56.2	6.2	0	0	50.0	0	0	0	0	0	50.0	25.0	25.0	0	0	50.0	0	0	0	50.0	100.0	0	0	31.3	0	12.5	0	18.8
Sodium gynocardate, 2%	43.7	0	6.2	0	37.5	12.5	0	0	6.2	6.2	56.2	12.5	43.7	0	0	43.7	0	0	6.2	37.5	100.0	6.2	6.2	12.5	0	0	12.5	0
Sodium hydnocarpate, 5%	37.5	0	0	0	37.5	25.0	25.0	0	0	0	62.5	37.5	25.0	0	0	37.5	0	0	0	37.5	100.0	0	0	31.3	0	18.8	0	12.5
Sodium hydnocarpate, 3%	33.3	0	0	0	33.3	33.3	33.3	0	0	0	60.0	60.0	0	0	0	33.3	0	0	0	33.3	93.5	6.7	0	20.0	0	0	0	20.0
Sodium hydnocarpate, 2%	18.7	6.2	12.5	0	0	31.2	18.7	6.2	6.2	0	100.0	43.7	56.2	0	0	12.5	6.2	6.2	0	0	100.0	25.0	43.7	6.2	6.2	0	0	0
Sodium morrhuate, 10% (our own)	37.5	6.2	6.2	6.2	18.7	18.7	6.2	6.2	6.2	0	75.0	37.5	37.5	0	0	18.7	0	0	6.2	12.5	100.0	12.5	31.3	12.5	6.2	0	0	6.2
Sodium morrhuate, 5% (our own)	26.7	0	6.7	0	20.0	13.3	6.7	0	6.7	0	73.4	33.3	33.3	6.7	0	33.3	0	0	0	33.3	100.0	6.7	20.0	13.3	6.7	6.7	0	0

duced some injury to the internal elastic lamina in 31.3 per cent of the sections. Others of the sclerosing substances produced injury to the lamina in smaller percentages even to 2 per cent sodium hydnocarpate, which produced injury to the lamina in the smallest number of sections (6.2 per cent).

CHANGES IN THE MEDIA

Edema.—This change was the most frequent one observed in the media. The highest percentage of edema (75 per cent) occurred in the veins into which 3 per cent sodium gynocardate and 3 per cent sodium hydnocarpate were injected. The lowest percentage of edema of the media (36 per cent) occurred in vessels into which Searle's sodium morrhuate was injected. In the veins into which the latter substance was injected, however, we noted coagulation necrosis or complete destruction of the media in 42 per cent of the sections, and in these instances edema was absent.

Hemorrhage was found in the media more often (20 per cent) in the sections of veins into which 3 per cent sodium hydnocarpate was injected than with any other substance. There was no hemorrhage in any of the sections of veins into which Searle's sodium morrhuate was injected. As has been stated previously, this substance produces a high percentage of a more profound change-coagulation necrosis. Sodium gynocardate (5 per cent), next to Searle's sodium morrhuate the most efficient thrombus-producing drug in our series, produced hemorrhage in the media in only 6.2 per cent of the veins into which it was injected.

Leukocytic Infiltration.—Leukocytic infiltration was found in the media in a small percentage of instances after the intravenous injection of each of the nine solutions studied by us. The leukocytes were usually not found in abundance. Sometimes, however, the infiltration was marked (fig. 10). Sodium hydnocarpate, 5 per cent, gave the highest percentage of leukocytic infiltration in the media (31 per cent). When this change was found, thrombosis usually had occurred.

Connective Tissue Proliferation.—This change was not an immediate one. Fibroblasts were noted in the media in some instances in sections removed as early as forty-eight hours. There was marked variation in the percentage of connective tissue proliferation produced by the different substances in this series. The percentage varied from 6.7 in the instance of 2 per cent sodium hydnocarpate to 62.5 for 5 per cent sodium gynocardate. The presence of connective tissue in excess in the media was noted in the vessels showing thrombi that had been present for some time and was more marked in the vessels showing organized thrombi. An increase of connective tissue in the media closely

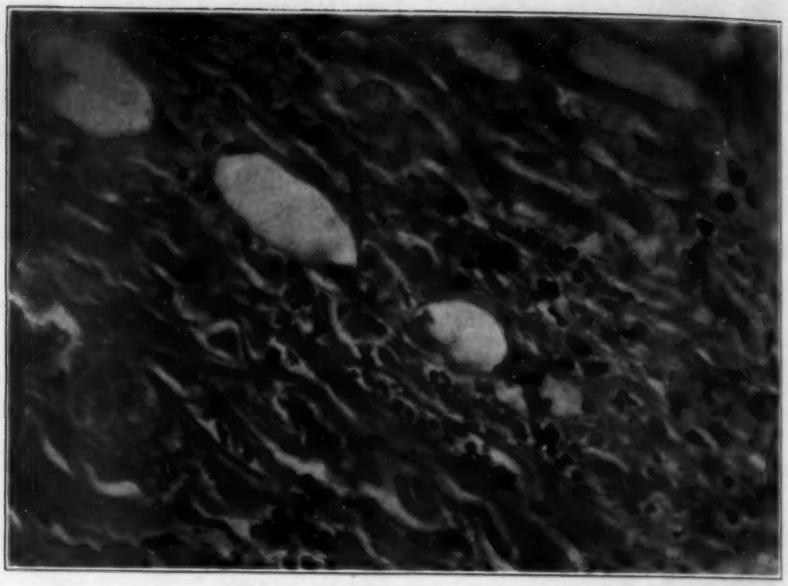

Fig. 10.—Photomicrograph of a vein showing leukocytic infiltration in the media forty-eight hours after the injection of Searle's sodium morrhuate.

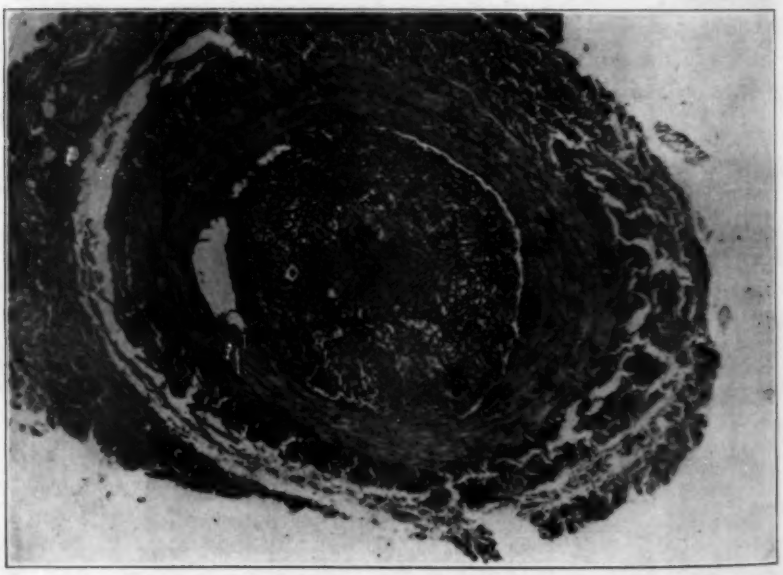

Fig. 11.—Photomicrograph of a vein showing an organized thrombus four weeks after the injection of Searle's sodium morrhuate.

paralleled the same change in the adventitia, as may be observed in tables 2 and 3. It is an indication of repair of injury to the media.

New Blood Vessels in the Media.—Normally in the peripheral vein of the dog there are no vessels in the media other than capillaries. When the vein is occluded by a thrombus, new vessels form in the media as well as through the clot in an attempt to reestablish a collateral circulation and also apparently in some instances in reaction to injury. The finding of new vessels in the media closely paralleled the finding of an occlusion of the lumen. In the instance of 5 per cent sodium gynocardate, 50 per cent of the sections showed new blood vessels in the media. Sections of vein removed after injecting our own sodium morrhuate (10 per cent) showed no new vessels in the media in any instance, but in only one section of those removed after twelve hours was the lumen occluded by a thrombus. Thus the appearance of new vessels in the media is an accompaniment of any thrombosis and together with the recanalization of the clot represents a reparative process in the reestablishment of circulation through new channels.

Coagulation Necrosis.—Searle's sodium morrhuate produced the most profound changes in the wall of the vein of all the substances we used. In 42.8 per cent of the sections of veins into which this substance had been injected there was evidence of injury of the muscle of the media to the extent even of presenting a glazed homogeneous, dull-staining, non-nucleated stratum of tissue, in which apparently the muscle cells had undergone necrosis (fig. 9). We did not determine the character of the reparative process which resulted in the recovery from this change in our sections, but the apparent necrosis did not seem to persist as it was not observed in sections removed after three days. Apparently the cells were injured but not completely destroyed, and were able to recover as there was no evidence of their being replaced by connective tissue in sections removed after longer periods. This change, therefore, cannot be considered an undesirable one because it does not interfere with normal processes of reaction to the sclerosing substance. On the other hand, it is probably of therapeutic value, because wherever coagulation necrosis in the media was found, a thrombus completely occluded the lumen of the vein. Although thrombosis occurred without coagulation necrosis, the latter was always accompanied by thrombosis. Coagulation necrosis also occurred in veins into which other substances had been injected; 5 per cent sodium hydnocarpate produced it in 18.8 per cent of the veins, but 5 per cent sodium gynocardate in no instance.

Atrophy of the Muscle.—In some instances in which there was an organized clot present the muscle cells seemed to be small and the nuclei elongated. This apparent atrophy was noticeable when a fibrous clot occluded the lumen and when there was evidence of an increase in the

TABLE 2.—*Degree and Incidence of Changes in Media After Intravenous Injections of Nine Different Sclerosing Solutions*

	Edema					Leukocytic Infiltration					Hemorrhage					Connective Tissue Proliferation					New Blood Vessels					Coagulation Necrosis	Muscle Atrophy
	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%		
Sodium morrhuate, 5% (Searle)	71.4	35.6	21.3	14.2	0	14.2	7.1	7.1	0	0	0	0	0	0	0	21.3	14.2	7.1	0	0	7.1	0	7.1	0	0	42.8	14.2
Sodium gynocardate, 5%	62.5	56.3	0	62.0	0	18.8	12.5	0	0	6.2	6.2	0	6.2	0	0	62.5	0	37.5	25.0	0	50.0	43.7	6.2	0	0	0	0
Sodium gynocardate, 3%	87.5	75.0	12.5	0	0	25.0	0	25.0	0	0	18.8	0	6.3	6.3	6.3	31.3	25.0	6.3	0	0	18.8	6.3	6.3	6.3	0	6.4	18.2
Sodium gynocardate, 2%	68.7	56.2	6.2	6.2	0	12.5	0	6.2	6.2	0	12.5	0	6.2	6.2	0	25.0	12.5	12.5	0	0	12.5	6.2	6.2	0	0	12.5	6.2
Sodium hydnocarpate, 5%	75.0	50.0	25.0	0	0	31.1	12.2	18.8	0	0	0	0	0	0	0	12.5	12.5	0	0	0	12.5	6.2	6.2	0	0	18.8	12.5
Sodium hydnocarpate, 3%	86.6	73.3	0	13.4	0	26.7	13.4	0	13.4	0	20.0	0	20.0	0	0	13.4	13.4	0	0	0	13.4	13.4	0	0	0	0	13.4
Sodium hydnocarpate, 2%	82.3	62.5	18.8	0	0	6.2	6.2	0	0	0	0	0	0	0	0	31.2	18.7	12.5	0	0	0	0	0	0	0	0	0
Sodium morrhuate, 10% (our own)	93.5	68.8	25.0	0	0	12.2	0	12.2	0	0	0	0	0	0	0	12.2	0	12.2	0	0	0	0	0	0	0	0	0
Sodium morrhuate, 5% (our own)	50.7	53.0	6.7	0	0	6.7	0	6.7	0	0	6.7	6.7	0	0	0	6.7	6.7	0	0	0	6.7	6.7	0	0	0	6.7	0

TABLE 3.—*Degree and Incidence of Changes in Adventitia After Intravenous Injections of Nine Different Sclerosing Solutions*

TABLE 3.—*Degree and Incidence of Changes in Adventitia After Intravenous Injections of Nine Different Sclerosing Solutions*

	Edema					Hemorrhage					New Vessels					Leukocytic Infiltration					Hyperemia					Connective Tissue Proliferation				
	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%	Total	0-25%	25-50%	50-75%	75-100%
Sodium morrhuate, 5% (Searle)	100.0	50.0	42.9	7.1	0	35.6	7.1	14.2	14.2	0	7.1	0	7.1	0	0	42.8	21.3	14.2	7.1	0	50.0	7.1	28.5	14.2	0	7.1	0	7.1	0	0
Sodium gynocardate, 5%	50.0	50.0	0	0	0	0	0	0	0	0	43.8	43.8	0	0	0	25.0	12.5	12.5	0	0	62.6	43.8	18.8	0	0	50.0	50.0	0	0	0
Sodium gynocardate, 3%	87.5	37.5	37.5	12.5	0	6.5	6.5	0	0	0	25.0	0	25.0	0	0	25.0	0	12.5	12.5	0	56.2	12.5	43.7	0	0	37.5	37.5	0	0	0
Sodium gynocardate, 2%	56.2	25.0	25.0	6.2	0	0	0	0	0	0	0	0	0	0	0	18.7	6.2	12.5	0	0	68.7	62.5	6.2	0	0	6.2	0	6.2	0	0
Sodium hydnocarpate, 5%	75.0	50.0	25.0	0	0	6.2	0	6.2	0	0	37.5	31.3	6.2	0	0	25.0	18.8	6.2	0	0	50.0	18.8	25.0	0	6.2	25.0	25.0	0	0	0
Sodium hydnocarpate, 3%	86.0	73.5	13.4	0	0	0	0	0	0	0	13.4	13.4	0	0	0	26.7	13.4	13.4	0	0	26.7	20.0	6.7	0	0	6.7	6.7	0	0	0
Sodium hydnocarpate, 2%	75.0	75.0	0	0	0	12.5	0	12.5	0	0	6.2	6.2	0	0	0	6.2	0	6.2	0	0	31.2	25.0	6.2	0	0	6.2	6.2	0	0	0
Sodium morrhuate, 10%(our own)	100.0	31.3	62.5	6.7	0	6.1	0	0	6.7	0	6.7	0	6.7	0	0	18.8	12.2	6.7	0	0	62.5	25.0	37.5	0	0	18.8	6.7	12.2	0	0
Sodium morrhuate, 5% (our own)	100.0	73.3	26.6	0	0	26.7	0	20.0	6.7	0	6.7	6.7	0	0	0	40.0	20.0	20.0	0	0	53.4	26.7	26.7	0	0	0	0	0	0	0

interstitial connective tissue in the media. We interpret this as an expression of disuse. It was observed most commonly (18.2 per cent) in the sections of veins into which 3 per cent sodium gynocardate was injected. Only three sections of veins into which the latter drug was injected showed it. They were the veins removed after six, ten and fourteen days. These all had thrombi in the lumen, but no other veins removed later than six days after injection of this same substance showed thrombosis. Searle's sodium morrhuate produced atrophy of the muscle in 14.2 per cent of the sections. This is not a characteristic difference in the drugs but an indication of thrombosis that has occurred at some time prior to six days before removal, permitting sufficient time for atrophy to occur.

CHANGES IN THE ADVENTITIA

The changes in the adventitia resulting from the intravenous injection of sclerosing substances are chiefly those that might be expected in reaction to an irritant. In some instances they were marked; in others, mild, even though thrombosis might have occurred (table 3). Two changes (hemorrhage and leukocytic infiltration) were of especial significance, as they were almost invariably accompanied by thrombotic occlusion of the lumen. This was also evident in the investigation by Garside and one of us (A. O.).[1] Only occasionally were hemorrhage and leukocytic infiltration present without a thrombus.

Hemorrhage in the adventitia was observed most frequently (35.6 per cent) in the sections of veins into which Searle's sodium morrhuate was injected. It was not observed in any instance in the veins into which 5 per cent sodium gynocardate was injected. The sodium morrhuate, as was demonstrated in the media and the intima, produced more profound changes in the vessel than the 5 per cent sodium gynocardate, though the latter was scarcely less efficient in producing a thrombus.

Leukocytic infiltration of the adventitia occurred more frequently than hemorrhage. Leukocytic infiltration was found in 42.8 per cent of the veins into which Searle's sodium morrhuate was injected, and in 25 per cent of the veins into which sodium gynocardate (5 per cent) was injected. This change was seldom found after the third day, though it was observed in one instance as late as the twenty-first day.

Edema of the adventitia was frequently found. It was most marked in the early periods and decreased in the longer periods. It was present in all the veins into which Searle's sodium morrhuate was injected, though it was graded only as I (questionable) in 50 per cent of these instances. It was observed in half the veins into which 5 per cent sodium gynocardate was injected, and in no instance was it graded more than slight. All the other sclerosing substances showed edema of the adventitia in from 71 to 100 per cent of the sections.

Hyperemia of the vessels of the adventitia as manifested by dilatation and engorgement was present in sections removed at varying periods after injection. It was found in from 27 per cent (3 per cent sodium hydnocarpate) to 69 per cent (2 per cent sodium gynocardate) of the section. In some instances it represents reaction to inflammation, and in some instances undoubtedly an attempt to open the collateral blood channels.

New blood vessels and connective tissue proliferation in the adventitia are changes that closely parallel each other, as may be seen in table 3. This is to be expected. New vessels are attempts to form collateral circulation and were found in the vessels showing thrombosis that had been present forty-eight hours or longer. In three instances (our own 10 per cent sodium morrhuate, 5 per cent sodium hydnocarpate and 2 per cent sodium hydnocarpate) there was a suggestion of new vessel formation in the adventitia in forty-eight hours. This change was not observed to be sufficiently marked to grade it distinctly, however, before the fourth day (3 per cent sodium gynocardate). The percentage of new vessels in the media closely approximates the percentages of the same change in the adventitia, as may be observed in tables 2 and 3.

Connective tissue proliferation in the adventitia is an expression of repair. It was observed most commonly and most markedly in sections showing occlusion of the lumen by thrombosis.

Coagulation necrosis of cells of the adventitia was observed in a few instances (Searle's sodium morrhuate, once; 3 per cent sodium gynocardate, once; 10 per cent sodium morrhuate [our own], twice; 5 per cent sodium hydnocarpate, twice). This change was observed only in some parts of the adventitia of these vessels, and not throughout the entire coat. When it was present there was generally definite evidence of the presence of the sclerosing substance in the adventitia. In some of these instances we observed in the adventitia a brownish-yellow dull homogeneous substance that was undoubtedly the sclerosing substance. Probably in these instances there was some perivenous infiltration on the injected substance.

SUMMARY

Dogs were used as test animals to study the changes produced in veins by the intravenous injections of sclerosing substances and to determine the most efficient sclerosing solution. The method used was the same as that employed by Garside and one of us (A. O.),[1] and the results of the two studies are compared for thrombus-producing effectiveness. Nine solutions were investigated: 5, 3 and 2 per cent sodium gynocardate; 5, 3 and 2 per cent sodium hydnocarpate; 10 and 5 per cent sodium morrhuate (our own), and 5 per cent sodium morrhuate in benzyl alcohol (Searle). The results are given in percentages and

grades of changes found microscopically in sections of veins removed at sixteen time intervals from one-half hour to eight weeks. Searle's sodium morrhuate was the most efficient thrombus producer not only for our series, but also in a previous study [1] of twenty solutions. Sodium gynocardate, 5 per cent, was the next most efficient thrombus producer. Quinine and urea hydrochloride (from the earlier study) was only eighth in thrombus-producing effectiveness.

CONCLUSION

Experimental study on veins of dogs shows that sodium morrhuate (Searle) is the most efficient thrombus-producing solution of nine sclerosing solutions studied by us and twenty sclerosing solutions studied in a previous experiment.[1] Sodium gynocardate, 5 per cent, is the next most efficient intravenous sclerosing substance.

Destruction of the endothelium of a vein is the essential factor in the production of thrombus by a sclerosing agent.

THORACOGENIC SCOLIOSIS

INFLUENCE OF THORACIC DISEASE AND THORACIC OPERATIONS ON THE SPINE

J. DEWEY BISGARD, M.D.
OMAHA

In recent years the more critical study of disease of the thorax and the extensive development of radical surgical treatment in suitable cases of pulmonary tuberculosis, bronchiectasis and similar conditions have directed attention but insufficient interest to the influence of thoracic disease and thoracic operations on the spinal column. This group of cases also provides an unusual opportunity for an investigation of the mechanics of the thoracic spine. To determine the mechanical factors involved in the production, frequency, clinical significance and prevention of thoracogenic curvatures, 518 patients with various forms of thoracic disease and 336 patients operated on for thoracic disease were studied; the results of the investigation form the basis of this report.

It should be emphasized at the outset that these curvatures only occasionally become so extensive that they give rise to symptoms or a deformity of clinical significance, and that the terms "curvature" and "scoliosis" as used throughout this article merely designate deviations from the normal and not necessarily deformity of the spine.

The normal thoracic spine is maintained in a state of static equilibrium by a balance of the opposing forces acting on the two sides of the vertebrae. These forces are exerted not only by the ribs, muscles and ligaments and other soft tissues of the thoracic wall but by pressures and stresses which arise within the thoracic cage (pleural, intrapleural and pulmonary forces). An appreciable imbalance of any one of these factors is likely to result in a deviation, the mechanisms of which will be discussed under their respective headings.

In general, the likelihood of a curvature and the extent to which the spine deviates under the influence of imbalance depend on: (1) age, for the younger the subject the more responsive is the spine to imbalance; (2) extent of imbalance, which is determined by such factors as the location and duration of the disease and the type of surgical attack, and (3) a certain unexplained compensatory mechanism (possibly muscle tone) whereby in 2 comparable cases apparently with equal

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imbalance, slight or no deviation may develop in one patient, while an extensive deformity may develop in the other.

MECHANICAL ANALYSIS

Rib Imbalance.—The ribs are the principal agents for the support of the thoracic vertebrae by virtue of their rigidity not only as bony braces but also because of their service as instruments through which the forces exerted by the attached muscles and ligaments and the forces of intrathoracic pressures and stresses are transmitted to the vertebrae through their costovertebral articulations. Since the bony framework of the thorax is made up of a series of superimposed semirigid circular units, forces acting on one area are transmitted throughout the circumference of each unit. Normally each pair of ribs grips with pressure the vertebra with which it articulates. If this pressure is unequal on the two sides, or if it has been removed from one side by the extensive resection of ribs such as occurs in thoracoplastic operations (fig. 1 *A* and *B*), the unopposed ribs push the vertebrae toward the unsupported side, and a deviation results. A spine which was straight before operation will deviate with the convexity of the curve projecting into the side on which the operation was performed.

The degree to which this occurs depends on certain factors: (1) the number and length of the costal segments resected (fig. 1 *A* and *B*); resection of one small segment as in open drainage of an empyema cavity does not demonstrably influence spinal equilibrium; (2) the level of costal resections; as a rule much greater deviations result from the resection of the upper than from that of the lower ribs (fig. 1 *B* and *C*); (3) the proximity of the spine to the costal segments resected; as illustrated by figure 2, the closer to the spine the costal resection is carried, the greater is the deviation or the likelihood of a deviation. The removal of segments anterior to the angles of the ribs has slight or no influence on the spine. Apparently adequate support is maintained through the long residual posterior stumps and their important muscular attachments.

The curvatures which result from the imbalance produced by the resection of ribs may be designated as thoracoplasty scolioses (fig. 1 *A* and *B*). They usually involve only a short segment of the spine—as a rule, the upper thoracic segment—and they are often rather sharply angulated. With each successive stage of multistaged thoracoplasties the angle of the curvature is often slightly increased, and usually a more extensive segment of the spine becomes involved. When the stages progress downward from the upper to the lower ribs, the apex of the curve correspondingly moves downward slightly. Lateral deviations of considerable extent are accompanied by rotation of the vertebral

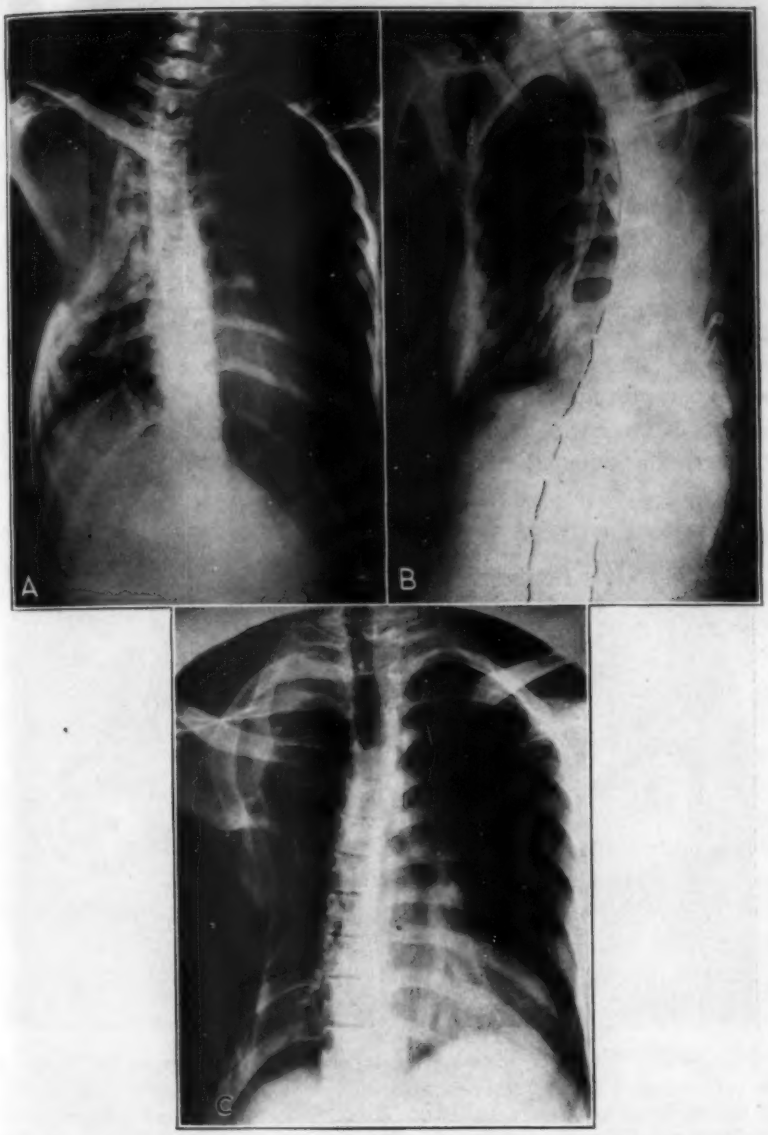

Fig. 1.—Thoracoplasty scoliosis illustrating rib imbalance: *A*, a short high dorsal dexter convex lateral curvature has developed in a previously straight spine as a result of the imbalance produced by the partial extrapleural posterolateral thoracoplasty. A large tuberculous cavernous lesion at the right apex was closed, and the disease arrested by the resection of long segments of the upper seven ribs. As in this case, most of the spinal deviations which develop with the extrapleural type of thoracoplasty in adults are so slight that they have little clinical importance. *B*, a retouched roentgenogram in a case of chronic empyema in which the patient was cured by thoracoplasty of the Schede type. Almost total costectomies of the third to the ninth ribs, inclusive, were done. A deforming curvature has been produced by the gross imbalance resulting not only from the extensive costal resections but from the wide excision of muscles and other soft tissues of the thoracic wall and of the restraining pleural scar. Before operation the spine deviated in the opposite direction. A pleural scoliosis therefore has been overcorrected and converted into a thoracoplasty scoliosis. *C*, in this case the spine deviated only slightly after a Schede thoracoplasty. The fourth to the ninth ribs, inclusive, were resected. The greater degree of curvature shown in *B* is probably caused by the more extensive resection of the upper ribs.

bodies and of the thoracic cage. As a result of this mechanical factor, the deformity resembles that of all other rotary scolioses, such as idiopathic and paralytic scoliosis, and differs from that of pleural scoliosis in which there is slight or no rotation of the vertebrae.

Contrary to the opinion of Nissen,[1] who stated that scoliosis due to a thoracoplasty develops several weeks after operation, it has been my observation that the deviations appear immediately or within a few days after the ribs have been removed. This fact has an important bearing on preventive therapy.

It is of interest that costal resections have been done for the purpose of correcting idiopathic scoliosis. Volkmann,[2] Hoffa,[3] Sauerbruch,[4]

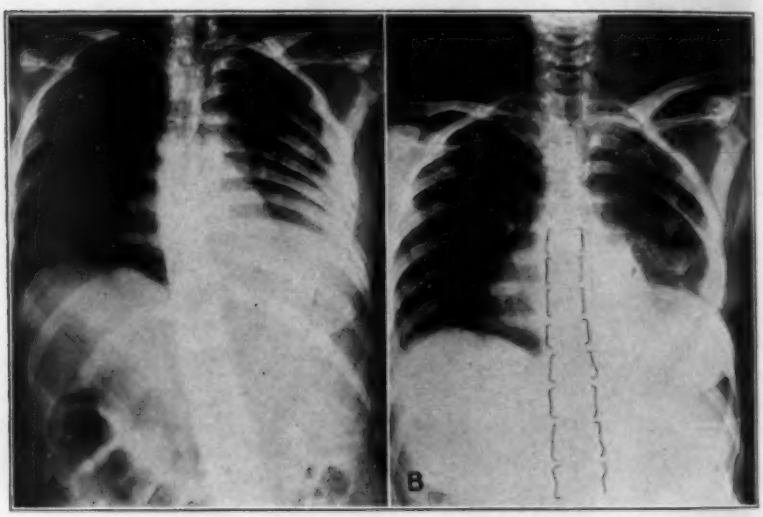

Fig. 2.—Rib imbalance, showing the influence of proximity to the spine: *A*, this patient had a pleural scoliosis associated with a mixed tuberculous empyema and osteomyelitis and chondritis of the overlying fifth, sixth and seventh ribs and costal cartilages. Resection of the anterior one third of these ribs and their cartilages did not alter the curvature. *B*, the same patient after a second operation, at which time the posterior segments of the same ribs were removed beyond their angles. The spine promptly straightened.

1. Nissen, R.: Mediastinalverlagerung bei postoperativer Skoliose und ihre praktische Bedeutung, München. med. Wchnschr. **75**:528, 1928.

2. Volkmann, R.: Rippenresection bei der Skoliose, Berl. klin. Wchnschr. **26**:1097, 1889.

3. Hoffa, A.: Operative Behandlung einer schweren Skoliose. Ztschr. f. orthop. Chir. **4**:402, 1895.

4. Sauerbruch, F.: Ueberlegungen zur operativen Behandlung schwerer Skoliosen, Arch. f. klin. Chir. **118**:550, 1921.

Loeffler,[5] Hoke,[6] Gaudier,[7] Casse,[8] Bade,[9] Lange [10] and others divided muscles and resected ribs on the side of the convexity or concavity or in both places, but their results have not encouraged a broad application of the principle.

Muscle Imbalance.—The influence of muscle imbalance in the production of spinal curvatures was pointed out by Leichtenstern [11] and is well illustrated by the paralytic scoliosis of anterior poliomyelitis and the spastic scoliosis of spastic hemiplegia. A mild spastic type of spinal curvature is observed often in cases of acute empyema (figs. 3 and 6*B*). As elsewhere in the body, nature attempts to immobilize and protect the acutely inflamed part by muscle spasm. The contracted muscles of the affected hemithorax and of the abdomen and neck on the same side narrow the intercostal spaces, draw the ribs downward and arch the spine with the concavity on the affected side. The spasm of the abdominal muscles may be so great that acute disease below the diaphragm is suspected.

The reverse type of deviation occurs as a result of the paralysis of a portion of the respiratory muscles produced by multiple intercostal neurectomy, an operation described by Alexander [12] and devised to give rest to a tuberculous lung. The second to the tenth intercostal nerves, inclusive, of one side are interrupted posteriorly to the rib angles.

To demonstrate the influence of muscle imbalance in the production of nonthoracogenic curvatures, Carey [13] devised an ingenious model of the vertebral column supported in equilibrium by the tension of rubber bands representing the principal opposing groups of muscles which act on the spine. By variously releasing the pull of certain bands he could

5. Loeffler, F.: Tenotomie der langen Rückenstrecker auf der Rippenbuckelseite bei Skoliosen, Zentralbl. f. Chir. **51**:825, 1924.

6. Hoke, M.: Study of a Case of Lateral Curvature of the Spine, Am. J. Orthop. Surg. **1**:168 (Nov.) 1903.

7. Gaudier, M. H.: Résection de la gibbosité costale comme adjuvant du traitement orthopédique de la scoliose, Bull. et mém. Soc. de chir. de Paris **46**: 1384, 1920.

8. Casse, J.: De la résection des côtes dans la scoliose, Ann. Soc. belge de chir. **4**:321, 1896.

9. Bade, P.: Rippenresektion bei schwerer Skoliose, Zentralbl. f. Chir **30**: 1045, 1903.

10. Lange, F.: Das Ergebnis einer ausgedehnten Rippenresektion auf der konkaven Seite bei einer schweren Skoliose, Ztschr. f. orthop. Chir. **41**:207, 1921.

11. Leichtenstern, quoted by Rey.[21]

12. Alexander, J.: Phrenicectomy and Intercostal Neurectomy for Pulmonary Tuberculosis, Ann. Int. Med. **4**:348 (Oct.) 1930.

13. Carey, E. J.: Scoliosis: Etiology, Pathogenesis and Prevention of Experimental Rotary Lateral Curvature, J. A. M. A. **98**:104 (Jan. 9) 1932.

produce curvatures with slight or great vertebral rotation and with deviation laterally toward or away from the side which had been released.

Arnd[14] produced curvatures in animals by resecting the erector spinae group of muscles of one side.

It would appear, however, that muscle imbalance plays a minor part in the production of thoracogenic curvatures. In all cases that I have observed the curvatures which presumably were produced solely by muscle imbalance were of minor degree and importance.

Intrathoracic Imbalance.—Unbalanced forces arising within the thorax may act directly on the spine. Contracting scar tissue, with

Fig. 3.—Muscle imbalance in a case of spastic scoliosis: The protective muscle spasm associated with an acute empyema in a child of 2 years has drawn the costal cage downward and narrowed the intercostal spaces. These factors have deviated the spine with the concavity on the side of the empyema.

anchorage to the thoracic wall laterally as a fixed point and to the movable spine mesially, may draw the vertebral bodies in the direction of the fixed point. Usually, however, the force is transmitted to the spine through the ribs.

For the sake of clarity, intrathoracic imbalance may be divided into three groups: pleural, intrapleural and pulmonary.

Pleural Imbalance; Pleural Scoliosis: The literature refers to this type of scoliosis as empyema scoliosis. I use the term "pleural scoliosis"

14. Arnd, J.: Experimentelle Beiträge zur Lehre der Skoliose, Arch. f. Orthop. u. Unfall-Chir. **1**:1, 1903.

because it describes more accurately the anatomic relationship and because the curvatures are often produced by pleural disease other than empyema. The pleural scar resulting from chronic pleuritis from any cause, such as a simple serous tuberculous effusion or tuberculous or nontuberculous empyema, contracts gradually and through adherence to the ribs pulls them centripetally. Since the ribs, like bucket handles, can pivot only at their extremities (the vertebral articulations posteriorly and the cartilages anteriorly) and inscribe arcs as they are drawn mesialward, they also move downward. This force is transmitted to the vertebral bodies through their costovertebral articulations, traction being exerted on the uppermost thoracic vertebrae by the upper ribs, which are pulled downward, and pressure being exerted on the lower ones, especially on those at the apex of the curve. The result is a spinal deviation with the convexity of the curve projecting into the healthy side, directed reversely to that produced by thoracoplasty.

It is of interest that this present day concept of unilateral stress exerted on the spine by the pleural scar was first advanced in 1827 by Delpeck,[15] to whom has been credited the earliest recorded recognition of the influence of thoracic disease on the spine. Walther,[16] Drachter,[17] Laennec,[18] Ziemssen [19] and Gaugele [20] stated the belief that the unbalanced respiratory function of the two sides which results from a pleural effusion and the atelectatic lung is an important factor in deviating the spine. Gaugele [20] suggested that negative intrapleural pressures may retract the thoracic wall in cases in which an effusion is rapidly absorbed. Rey [21] stated that in certain instances the weight of the fluid causes the spine to deviate with the convexity on the affected side in order to shift the center of balance and thereby gain equilibrium. Obviously this explanation applies only to spines bearing superincumbent weight which produces a curve directed reversely to that which is almost invariably observed.

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15. Delpeck, J.: Ueber die Empyema, Abhandl. d. Akad. d. Wissench., Chir. de Montpellier **1**:3, 1827.

16. Walther, H.: Ueber die empyematische Skoliose, Ztschr. f. orthop. Chir. **26**:401, 1910.

17. Drachter, R.: Bedeutung der Interkostalmuskelatrophie beim Raumausgleich im Thorax und der Begriff der Lungenstützfunktion, München. med. Wchnschr. **66**:485, 1919.

18. Laennec, R.: Traité de l'auscultation médiate et des maladies des poumons et du cœur, Paris, J. C. Chaude, 1826.

19. Ziemssen, H.: Pleuritis und Pneumonie im Kindesalter, Berlin, Hirschwald, 1862.

20. Gaugele, K.: Die postpleuritische Skoliose und ihre Verhütung, München. med. Wchnschr. **66**:442, 1919.

21. Rey, J.: Die praktische Bedeutung der postpleuritischen Skoliose im Kindesalter, Arch. f. Kinderh. **72**:261, 1922.

The nature of the etiology of pleural scoliosis makes it a distinct clinical entity. It differs from all of the other types in that there is no or slight rotation of the vertebral bodies. This disobedience to the well recognized physical law (stressed by Lovett [22]) of the dissipation of part of the bending force of rods into the production of rotation or twisting is due to the immobilization of the ribs in their retracted positions. The vertebrae cannot rotate against the resisting pressure exerted on them by the ribs, which are rigidly fixed by the pleural scar. This scar in certain instances undoubtedly exerts force directly on the verte-

TABLE 1.—*Comparative Measurements of Thoracic Circumference in Five Consecutive Cases of Empyema with Scoliosis*

Patient	Type of Empyema	Age	Side of Empyema	From Midsternum	To Spinous Process	Hemithorax, Inches: Right	Hemithorax, Inches: Left
C. T.	Acute	2	Left	2d rib	5th spinous process	9	8
				4th rib	7th spinous process	9⅜	8
				Tip of ensiform process	12th spinous process	9⅜	9½
K. D.	Acute	7	Left	2d rib	5th spinous process	12½	11¼
				4th rib	7th spinous process	12¾	11½
				Tip of ensiform process	12th spinous process	12½	12½
J. K.	Chronic	22	Right	2d rib	5th spinous process	14¾	17½
				4th rib	7th spinous process	14¾	17¾
				Tip of ensiform process	12th spinous process	17¼	19½
J. B.	Chronic	24	Left	2d rib	5th spinous process	16½	13¾
				4th rib	7th spinous process	17	14
				Tip of ensiform process	12th spinous process	17	14¼
D. C.	Chronic	14	Right	2d rib	5th spinous process	12¼	14½
				4th rib	7th spinous process	12½	15¼
				Tip of ensiform process	12th spinous process	12¾	15

The maximum difference in the circumference of the two sides was 3 inches (7.6 cm.). Greater reductions in expansion occurred in the cases of chronic than in the cases of acute empyema. Von Kölliker [23] and Apert (Bull. Soc. de pédiat. de Paris **10**:277, 1908) reported cases with slightly greater differences in the two sides.

bral bodies, which helps to prevent rotation and usually also fixes the mediastinum to the spine so that it deviates with the spine.

The retraction of the thoracic wall by scar tissue restricts the respiratory excursions and greatly reduces the volume capacity of the affected hemithorax. Comparative measurements of the circumference of the two halves of the thorax in 5 cases are compiled in table 1.

The influence of the pathogenesis of pleural scoliosis on the clinical picture which it produces is brought out effectively by comparing it with that of idiopathic scoliosis, as is presented in table 2, the drawings of figure 4 and the roentgenograms of figure 5 *A* and *B*.

22. Lovett, R.: The Element of Torsion in Lateral Curvature of the Spine, Am. J. Orthop. Surg. **1**:353, 1903.

Intrapleural Imbalance: If the mediastinum is fixed so that it cannot shift to compensate for changes of intrapleural pressures on the two sides, unequal pressures can be maintained within the pleural cavities, and this imbalance may make itself felt on the spine through the medium of the thoracic wall and may result in a spinal deviation. In 3 of 102

TABLE 2.—*Comparison of Deformities* *

Pleural Scoliosis	Idiopathic Scoliosis
1. On the side of the concavity	1. On the side of the concavity
a. Increased downward inclination of the ribs; pulled downward and mesialward by pleural scar	a. Abnormally horizontal position of ribs; since the ribs rotate with the vertebra toward the side of convexity their arched shapes cause them to lift upward
b. Intercostal spaces narrowed; ribs contact or overlap and fuse	b. Intercostal spaces unchanged or only slightly narrowed
c. Thoracic wall (costal arches) flattened anteriorly and posteriorly	c. Thoracic wall (costal arches) flattened posteriorly but bulged anteriorly, owing to vertebral rotation
d. As a result of the retraction of the ribs, hemithorax smaller than that on the opposite or convex side; the circumference from 1¾ to 3 inches (3.5 to 7.62 cm.) smaller in five cases measured (table 1)	d. As ribs rotate upward and outward this hemithorax becomes larger than that of the opposite or the convex side
e. Lung on this side relaxed and atelectatic	e. Lung on this side partially emphysematous and partially atelectatic
2. On the side of the convexity	2. On the side of the convexity
a. No posterior bulge of thoracic wall because there is no rotation deformity	a. Thoracic wall (costal arches) flattened anteriorly and bulged posteriorly at apex of curve, owing to rotation of vertebrae
b. Shoulder high but scapula not prominent	b. Shoulder high and scapula prominent
3. Either no or only slight rotation and structural change of vertebral bodies †	3. Always rotation and often great; usually structural changes (wedging)
4. Curves usually rigid and often short and sharply angulated	4. Frequently not rigid and often long and gently arched
5. Often compensatory curvatures do not develop until the patient sits up and the spine bears weight	5. Patients are ambulatory, so compensatory curvatures frequently develop simultaneously with the primary curves
6. Mediastinum usually deviates with the spine, to which it is fixed by scar tissue	6. Mediastinum does not deviate; it is free and maintains its normal position
7. Reduction of vital capacity proportional to deformity (Flagstad and Kollman: J. Bone & Joint Surg. **10**: 724, 1928)	7. Same

* Compare with figures 4 and 5.

† Walther[16] investigated pleurogenic scoliotic spines and reported that: 1. Rotation of the vertebrae is slight or absent. 2. Only slight wedge formation of vertebral bodies occurs, but often there is a pronounced concave compression of the intervertebral disks. 3. The transverse processes present changes due to torsion.

cases of acute empyema there were extremely massive effusions which displaced the mediastinum far into the healthy side and as a result produced marked respiratory embarrassment. In these 3 cases the spine deviated with the convexity pointing toward the side on which the empyema occurred, the reverse of the direction of the curvatures observed in all of the other cases of acute empyema. They differed also in that the intercostal spaces were distinctly wider than normal. Two theoretical explanations are possible: 1. The mobile mediastinum may

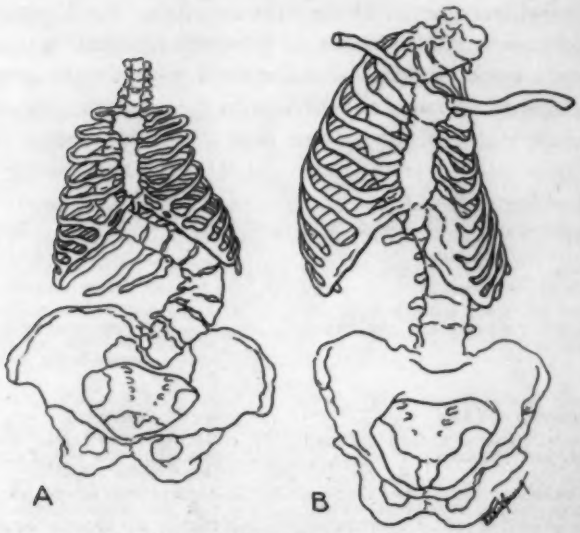

Fig. 4.—Diagrammatic drawings illustrating table 2, for a comparative analysis of rotary and nonrotary scoliosis. To the left is illustrated the rotation deformity of the thorax of idiopathic scoliosis, which typifies the rotary type of scoliosis. The drawing to the right represents the deformity of pleural scoliosis which uniquely is a nonrotary type of curvature (table 2).

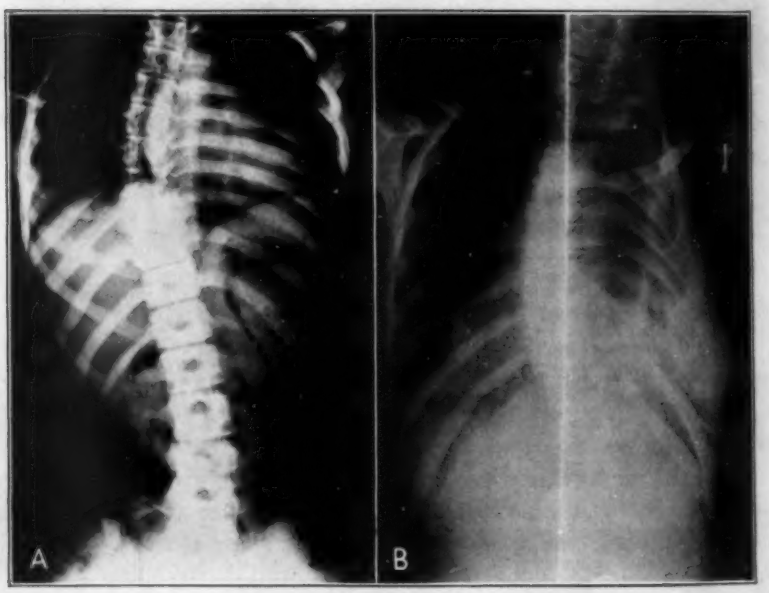

Fig. 5.—Roentgenograms in a case of (*A*) idiopathic scoliosis and (*B*) pleural scoliosis. Compare with figure 4 and table 2. Note that the mediastinum did not deviate with the spine in *A* but did deviate in *B*.

have been displaced by the massive effusion until its elastic recoil permitted an increase of the intrapleural pressure on the affected side sufficient to widen the intercostal spaces and deviate the spine in the direction opposite to that produced by the traction of muscle spasm. 2. It is possible that a voluntary effort was made by the patient to minimize the mediastinal displacement, and consequently the respiratory embarrassment, by increasing the capacity of the affected hemithorax by widening the intercostal spaces and deviating the spine in a favorable direction. The roentgenograms in 1 of these cases have been reproduced (fig. 6).

Occasionally, as is illustrated in figure 7, a pneumothorax maintained for a considerable length of time, with high or moderately positive pres-

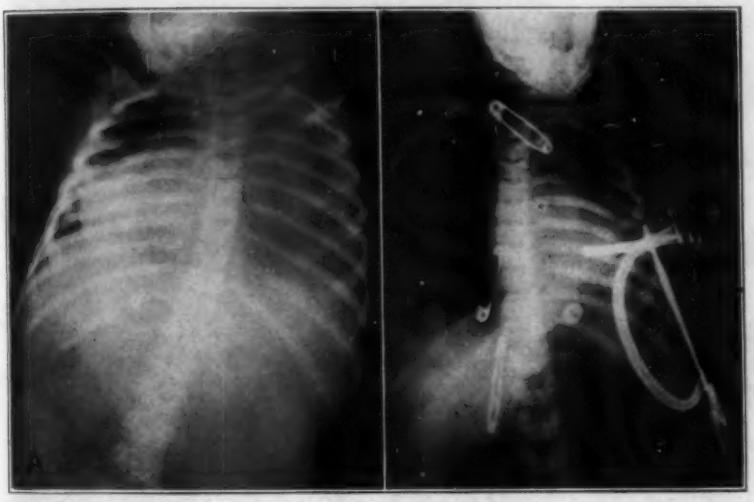

Fig. 6.—Intrapleural imbalance: *A*, an acute empyema of the left side with a massive effusion which has displaced the mediastinum far into the right side and diminished the available aerating lung to such an extent that the patient was cyanotic and dyspneic. Note the widening of the intercostal spaces on the left side and the spinal deviation with the convexity to the left. *B*, the same patient after drainage was established. Note the narrowing of the left intercostal spaces and the reversal of the spinal curvature, which is now of the spastic type characteristic of acute empyema.

sures against a fixed mediastinum, will produce the same deformity as that described earlier, namely, a widening of the intercostal spaces and a spinal deviation with the convexity on the side of the pneumothorax.

If the mediastinum has normal mobility it offers less resistance than do the thoracic cage and spine to unbalanced intrathoracic forces on the two sides, and it will shift into either side from its normal midline

position and within certain limits will prevent an imbalance. It compensates for unequal pressures on the two sides by increasing the volume of one hemithorax at the expense of the other in an endeavor to maintain the normal physiologic, less than atmospheric, intrapleural pressures.

Intrapulmonary Imbalance: The forces exerted by the lungs on the thoracic wall and transmitted through it to the spine are not infrequently unbalanced by such conditions as massive pulmonary atelectasis and emphysema and by extensive pulmonary fibrosis (fig. 8*A*). Again, the influence of these conditions on the spine depends to a large measure on the ability of the mediastinum alone to compensate for the unilateral or unbalanced stress.

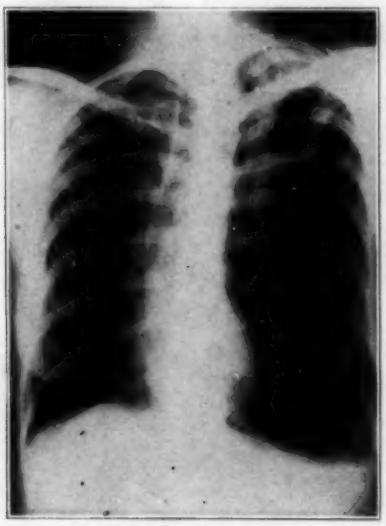

Fig. 7.—Intrapleural imbalance: A case of pulmonary tuberculosis with a large open cavity at the left apex which artificial pneumothorax therapy has failed to close because of adhesions which suspend the lung to the lateral thoracic wall. As a result of maintaining the intrapleural pressure considerably above atmospheric, the intercostal spaces of that side have been widened and the spine deviated with the convexity toward the side of the pneumothorax.

Pulmonary disease which has produced extensive parenchymal fibrosis frequently has extended to the pleurae and produced a pleuritis which often fixes the lung to all or any part of its bony and mediastinal encasement. Consequently, as the scar tissue in the lung contracts, stress is exerted on these attachments with three possible results: 1. If the mediastinum is mobile, it is pulled into the affected hemithorax, and since this pull takes place slowly and gradually, the mediastinum has time to stretch and may therefore shift to a remarkable degree (fig.

8*B*). 2. The pleural scar may produce a pleural scoliosis which diminishes the volume of the affected hemithorax and gives relaxation to the fibrosing lung. 3. If the lung is anchored to the vertebral bodies mesially and to the thoracic wall laterally, the force of contracture of the fibrosing lung not infrequently will pull the less resistant point of anchorage, the vertebral bodies, toward the fixed point, the ribs of the lateral thoracic wall. Since these ribs pass obliquely upward posteriorly and articulate with vertebrae above those to which the lung is anchored, the pull on these ribs is transmitted to the vertebrae in the form of pressure which pushes them in the direction opposite to those at the apex of the curve. In other words, the vertebrae and ribs in the direct line of force

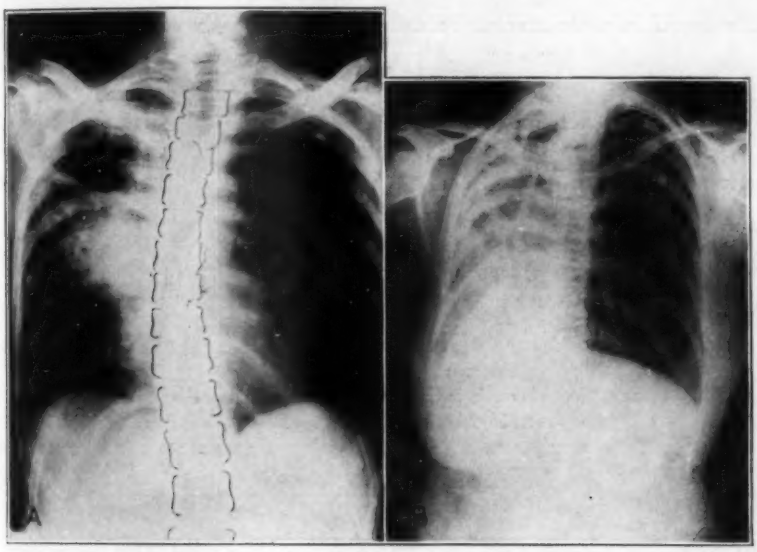

Fig. 8.—Pulmonary imbalance: *A*, a roentgenogram of a patient with far advanced pulmonary tuberculosis; a large right apical cavity and extensive parenchymal fibrosis are present. With the lung anchored to the thoracic wall laterally and to the vertebral bodies mesially by the scar of an associated pleuritis, the shrinkage of the fibrotic lung has pulled the movable vertebral bodies toward the fixed point, the lateral thoracic wall. *B*, in this case of pulmonary tuberculosis, the contracture of the fibrotic and atelectatic right lung has drawn the mediastinal structures into the right hemithorax. Note the complete dexter cardia, dexter displacement of the trachea and the compensatory emphysema of the left lung. In the absence of fixation to the spine, the mediastinum and left lung shifted to the right to balance the force of the shrinkage of scar tissue. The spine was therefore uninfluenced.

at the apex of the curve are pulled on directly, while the vertebrae immediately above the apex are acted on indirectly through the ribs. Figure 8*A* illustrates the result of the action of these forces.

CLINICAL CLASSIFICATIONS

In the following classifications, the curvatures have been grouped according to degree: (1) slight, or of no clinical significance; (2) moderate, a deviation of clinical importance without appreciable deformity, and (3) severe, or extensive curvatures with deformity. Obviously this grouping is merely relative.

Acute Empyema; Spastic Scoliosis.—In this investigation all cases of empyema of less than three months' duration have been classified arbitrarily as acute, and those of longer duration as chronic (fig. 3).

TABLE 3.—*Acute Nontuberculous Empyema; the Influence of Age on the Incidence and the Degree of Scoliosis*

	Right Empyema Sinister Convex Scoliosis (Degree)				Left Empyema Dexter Convex Scoliosis (Degree)					
Age, Years	Number Cases	None	Slight	Moderate	Number Cases	None	Slight	Moderate	Reversed Curves	Total Cases
0-10	23 (43.4%)	12 (52.1%)	7 (30.5%)	2 (8.7%)	17 (34.7%)	8 (47%)	6 (35.3%)	3 (17.6%)	2	40
10-20	11 (20.7%)	6 (54.5%)	5 (45.5%)	0	12 (24.5%)	6 (50%)	5 (41.6%)	0	1	23
20-30	10 (19%)	7 (10%)	3 (30%)	0	5 (10.2%)	3 (60%)	1 (20%)	1 (20%)	0	15
30+	9 (16.8%)	7 (77.7%)	1 (11.1%)	0	15 (30.6%)	9 (60%)	6 (40%)	0	1	24
Totals	53	32 (60%)	16 (30.1%)	2 (3.7%)	49	26 (53%)	18 (36.7%)	4 (8.1%)	4	102

TABLE 4.—*Acute Nontuberculous Empyema; the Influence of the Duration of the Disease on the Incidence and the Degree of Scoliosis*

	Degree of Scoliosis			
Duration of Disease	None	Slight	Moderate	Total
0 to 4 weeks	43 (62.3%)	23 (33.3%)	3 (4.3%)	69
4 to 12 weeks	11 (39.3%)	15 (53.5%)	2 (7.1%)	28
Totals	54 (55%)	38 (39%)	5 (6%)	97

One hundred and two cases of acute empyema were studied (tables 3 and 4). Forty-four presented spinal deviation, in 38 (86.4 per cent) of slight and in 6 (13.6 per cent) of moderate degree.

Empyema of the left side predominated slightly and was associated with a slightly greater incidence of spinal deviations. In all but 4 cases the spine deviated with the concavity on the affected side. Three of the 4 cases manifested extremely massive effusions; they were discussed in an earlier paragraph (fig. 6). In the other case there was a preexisting rachitic scoliosis. The influence of age on the incidence and degree of deviation was definite but not striking. In 40 patients with ages ranging below 10 years there was an incidence of 50 per cent as

compared with 30 per cent in 24 patients over 30 years of age. Likewise the duration of the disease increased the incidence of scoliosis from 37 per cent in cases observed within four weeks of the onset of the empyema to 60 per cent in those of longer duration.

Since the curvatures of acute empyema are produced mainly by muscle spasm, they usually correct themselves completely unless the disease progresses to chronicity.

Chronic Empyema; Pleural Scoliosis.—Since all of the pleural scolioses, regardless of etiology, present a typical clinical picture, comment

TABLE 5.—*Chronic Nontuberculous Empyema; the Influence of Age on the Incidence and the Degree of Scoliosis*

	Right Empyema Sinister Convex Scoliosis (Degree)				Left Empyema Dexter Convex Scoliosis (Degree)				Right and Left, Totals
Age, Years	Number Cases	None	Slight	Moderate	Number Cases	None	Slight	Moderate	
0 to 10.....	10 (23.2%)	3 (30%)	3 (30%)	4 (40%)	6 (10.1%)	1 (16.6%)	2 (33.3%)	3 (50%)	16
10 to 20.....	16 (37.2%)	4 (25%)	5 (31.2%)	7 (44.8%)	17 (28.8%)	4 (23.5%)	9 (53%)	4 (23.5%)	33
20 to 30.....	3 (7%)	2 (66.6%)	1 (33.3%)	0	14 (23.7%)	4 (28.5%)	6 (43%)	4 (28.5%)	17
30+.....	14 (32.5%)	9 (64.3%)	5 (35.7%)	0	22 (37.2%)	11 (50%)	7 (31.8%)	4 (18.8%)	36
Totals.....	43	18 (41.8%)	14 (32.5%)	11 (25.5%)	59	20 (34%)	24 (42.3%)	14 (23.7%)	102

TABLE 6.—*Chronic Nontuberculous Empyema; the Influence of the Duration of the Disease on the Incidence and the Degree of Scoliosis*

	Degree of Scoliosis			
Duration of Disease	None	Slight	Moderate	Total
3 to 6 months.....	13 (56.5%)	9 (39.1%)	1 (4.3%)	23
6 to 12 months.....	8 (36.3%)	8 (36.3%)	6 (27.3%)	22
Over 12 months.....	16 (30.7%)	17 (32.7%)	19 (36.5%)	52
Totals.....	37 (38%)	34 (35%)	26 (27%)	97

will be inclusive of the entire group of 146 cases of chronic empyema (figs. 5 *B* and 9 *A*). Of these, 102 (70 per cent) of the patients were nontuberculous (tables 5 and 6), and 44 (30 per cent) were tuberculous, the infections being pure and mixed (tables 7 and 8). Of the total group, curvatures developed in 95 (65.8 per cent); they were of slight degree in 61, moderate in 37 and severe in 2 per cent.

In all except 2 of the cases the spine arched with the concavity toward the affected side, and in these cases (tuberculous empyema) the reverse type of the curvature could be explained by mechanical factors incident to extensive pulmonary and pleural disease of the contralateral side.

As in the series of cases of acute empyema, there was a predominance of left-sided lesions (83 to 63), and the percentage incidence of scoliosis

was slightly greater in the cases of left-sided empyema. It is possible that the right lobe of the liver may resist the downward movement of the ribs on that side.

Rey [21] reported a study of 31 cases in which the patients were cured of chronic empyema by simple drainage. In 27 cases there were demonstrable scolioses, but in 2 of these cases the curvatures antedated

TABLE 7.—*Tuberculous Empyema; the Influence of Age on the Incidence and the Degree of Scoliosis*

	Empyema on the Right Side Sinister Convex Scoliosis (Degree)					Empyema on the Left Side Dexter Convex Scoliosis (Degree)					
Age, Years	Number Cases	None	Slight	Moderate	Moderately Severe	Number Cases	None	Slight	Moderate	Moderately Severe	Right and Left, Total
0-10	3 (15%)	0	2 (66.6%)	0	1 (33.3%)	2 (8.3%)	0	1 (50%)	0	1 (50%)	5
10-20	1 (5%)	0	1 (100%)	0	0	4 (16.6%)	2 (50%)	2 (50%)	0	0	5
20-30	10 (50%)	5 (50%)	2 (20%)	3 (30%)	0	9 (37.5%)	2 (22.2%)	5 (55.5%)	2 (22.2%)	0	19
30+	6 (30%)	2 (33.3%)	3 (50%)	0	0	9 (37.5%)	3 (33.3%)	4 (44.4%)	2 (22.2%)	0	15
Total	20	7 (35%)	8 (40%)	3 (15%)	1 (5%)	24	7 (29.3%)	12 (50%)	4 (16.6%)	1 (4.1%)	44

TABLE 8.—*Tuberculous Empyema; the Influence of the Duration of the Disease on the Incidence and the Degree of Scoliosis*

	Degree of Scoliosis				
Duration of Disease	None	Slight	Moderate	Moderately Severe	Total
0 to 4 weeks	4 (50%)	4 (50%)	0	0	8
4 to 12 weeks	3 (37.5%)	3 (37.5%)	2 (25%)	0	8
12 to 24 weeks	0	8 (66.6%)	3 (33.3%)	0	12
24 to 52 weeks	4 (40%)	5 (50%)	1 (10%)	0	10
More than 52 weeks	7 (43.8%)	1 (6.2%)	6 (37.5%)	2 (12.5%)	16
Total	18 (33.3%)	21 (38.8%)	12 (24%)	2 (3.7%)	54

the onset of the empyema. In all except 1 of the cases the spine deviated with the concavity on the affected side.

In the groups of acute and chronic empyema the incidence of scoliosis and the extent of deviation varied roughly in inverse proportion to the age of the patients and in direct proportion to the duration of the disease. The ratio in certain groups was almost 2:1 (tables 3 to 8).

Pulmonary Disease.—One hundred and eighty patients who had pulmonary tuberculosis uncomplicated by pleural effusions and who were not treated surgically were studied. The disease in most instances involved both lungs. In 32 (17.8 per cent) of the cases there was slight

but definite deviation of the spine, with the convexity of the curve directed to the side which was the more extensively diseased in 43.2 per cent and in the reverse direction in 56.8 per cent. Without exception, the deviations could be explained by one of the mechanical factors previously discussed: (1) extensive parenchymatous fibrosis with retraction of the thoracic wall, mediastinum and vertebral bodies; (2) extensive pleural involvement and the production of a pleural scoliosis, and (3) massive atelectasis in the presence of a fixed mediastinum (only 1 case).

Of the 48 consecutive cases of pulmonary abscess which were studied, 6 (12.5 per cent) were complicated by empyema, and in 4 (66 per cent) of these typical pleural scolioses had developed. In only 3 (7.1 per cent)

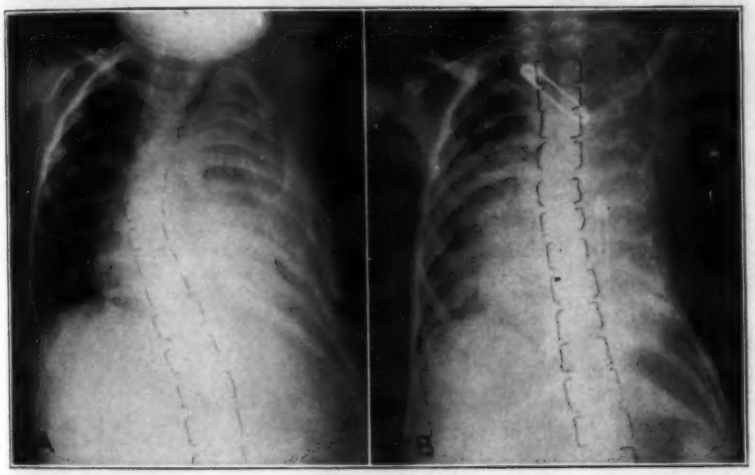

Fig. 9.—The influence of thoracic operations on the spine: *A*, a tuberculous empyema of two years' duration in a child of 4 years has been productive of a moderately severe pleural scoliosis. *B*, the same patient two weeks after completion of a Schede thoracoplasty. Note the correction of the pleural scoliosis by the imbalance produced by the operation.

of the remaining 42 uncomplicated cases was there evidence of spinal deviation, and in each of these there was evidence of retraction from extensive pulmonary fibrosis.

Forty-two unselected cases of bronchiectasis were studied; 5 (11 per cent) were complicated by empyema, and typical pleural scolioses had developed. Of the 37 uncomplicated cases, only 1 presented a deviation. In this case (fig. 11 *A* and *B*) the curvature could be explained only by assuming a certain instability which later permitted the spine to collapse completely as a result of a lobectomy.

From these data it is apparent that pulmonary disease seldom produces an imbalance capable of deviating the spine unless there is extensive pulmonary fibrosis or involvement of the pleura.

INFLUENCE OF THORACIC OPERATIONS

Although various surgical operations on the thorax may disturb the static equilibrium of the spine, only those involving extensive resection of the ribs, and the lobectomies produce deformities of clinical importance.

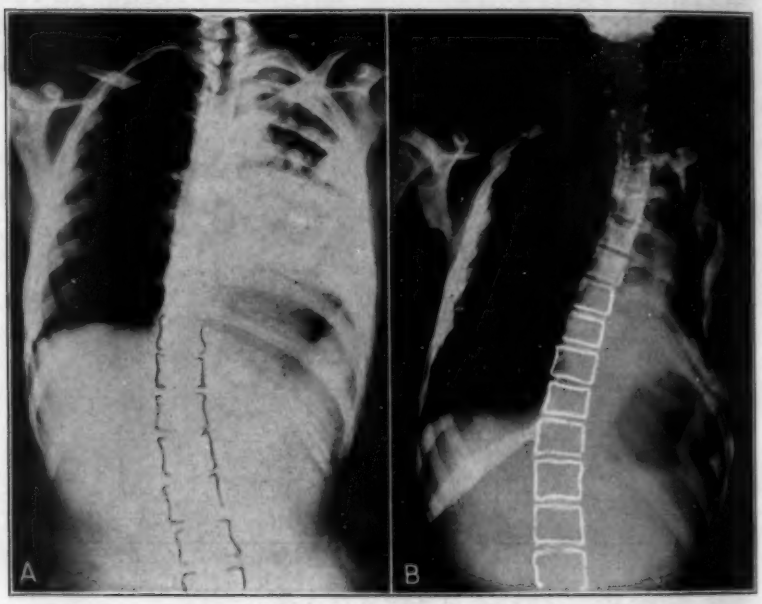

Fig. 10.—The influence of thoracic operations on the spine: *A*, the roentgenogram of a patient with multiple pulmonary abscesses of the lobes of the left lung complicated by empyema. Pleural scoliosis has developed. *B*, the same patient after completion of a total posterolateral thoracoplasty. A high dorsal thoracoplasty scoliosis has been superimposed on the pleural scoliosis, giving rise to a double or S-shaped curve.

Thoracoplasty.—A study of 131 patients treated by thoracoplasty showed that the contour of the spine is always altered, but that this alteration is influenced by the preoperative contour.

1. A spine which was straight previous to operation almost invariably deviated with the convexity toward the side on which operation was performed. This occurred in 59 (45 per cent) of the cases (fig. 1).

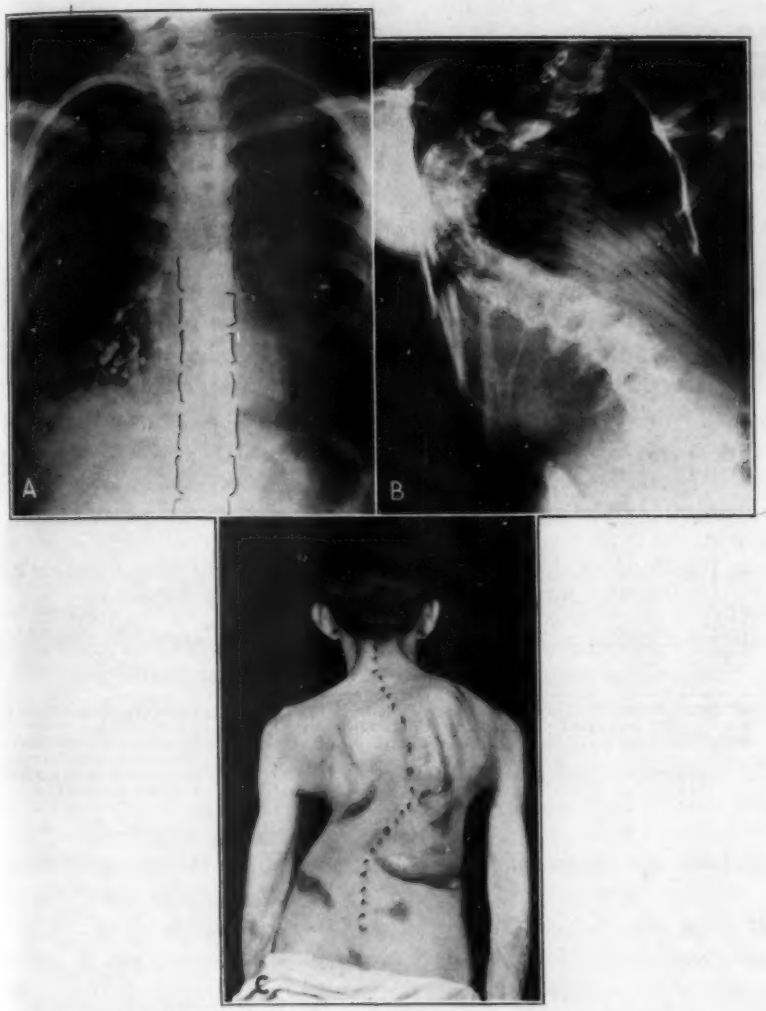

Fig. 11.—The influence of thoracic operations on the spine: *A*, roentgenogram of a patient with bronchiectasis of the right lower lobe, which has been filled with iodized poppy-seed oil, 40 per cent. Note the slight sinister convex scoliosis. *B*, the same patient three years after total excision of the right lower lobe. The spine has reversed its curvature and completely collapsed into the side on which operation occurred. Note the rotation of the vertebrae and the deformity of the thoracic wall caused by the rotation. *C*, photograph of the same patient illustrating the characteristic deformity of rotary scoliosis.

2. If it deviated with the convexity toward that side before operation the curvature was greatly exaggerated by thoracoplasty. This occurred in 21 cases (16 per cent).

3. If, however, it curved in the opposite direction (preoperative pleural scoliosis), the deviation was partially or completely corrected. This occurred in 12 (9 per cent) of the cases (fig. 9). Often the contour was overcorrected; this occurred in 39 (29 per cent) of the cases (fig. 11). In 5 cases a double or S-shaped curve developed, composed of a thoracoplasty curvature superimposed on a preexisting pleural scoliosis (fig. 10 *A* and *B*).

TABLE 9.—*The Influence of Extrapleural Thoracoplasty on the Spinal Column in One Hundred and One Cases*

		Preoperative Scoliosis			Postoperative Scoliosis		
	Degree	Right	Left	Straight Spine	Right	Left	Straight Spine
A. Right thoracoplasties (41 cases)	Slight.....	9	4	22	6	0	1
	Moderate....	0	2	0	32	0	0
	Totals.....	9	6	22	38	0	1
B. Left thoracoplasties (60 cases)	Slight.....	11	7	31	0	13	1
	Moderate....	4	..	..	0	46	..
	Totals.....	15	7	31	0	59	1

TABLE 10.—*The Fate of Curvatures of Pleural Scoliosis in One Hundred and Five Patients with Subacute and Chronic Empyema Treated by Thoracoplasty and Simple Drainage*

Simple Drainage (69 Cases)			Thoracoplasty (36 Cases)		
No change in curvature (26 cases)	Progression of curvature (26 cases)	Correction of curvature (17 cases)	Partial correction (2 cases)	Complete correction (8 cases)	Overcorrection (26 cases)
					Double or S-shaped curves Thoracoplasty curvatures superimposed on a pleural scoliosis (5 cases)

Of the 131 thoracoplasties, 101 were extrapleural and were carried out in the treatment of pulmonary tuberculosis. The remaining 30 operations were Schede thoracoplasties for empyema; the intercostal soft tissues and much of the parietal pleural scar were excised as well as the ribs. As a result of this additional resection (soft tissues and restraining parietal pleura), the Schede type of operation (fig. 1 *B*) as a rule produced greater imbalance and greater alteration of spinal contour than did the extrapleural type.

Before operation, in the group of 101 patients treated by extrapleural thoracoplasty there were 53 with straight spines and 48 with curvatures. Only 2 of the 101 patients had straight spines after operation, which effected complete correction of the preoperative curvatures (table 9).

Of the 30 patients treated by the Schede type of thoracoplasty, 5 had straight spines, 10 had slight deviations, and 8 had moderate curvatures before operation. After operation there were 7 patients with straight spines representing corrections of previous curvatures and 7 with slight, 9 with moderate and 2 with moderately severe overcorrections. Double curvatures developed in 3 cases, the original preoperative deviations remaining unchanged except for the overcorrection of the upper dorsal segments.

The morphologic characteristics of thoracoplasty scoliosis have been considered under the topic of rib imbalance.

Simple Drainage of Empyema Cavities.—The rapid obliteration of the cavities in acute empyema by early adequate dependent drainage prevents extensive fibrosis of the pleurae and consequently prevents pleural scoliosis. In 43 cases of acute empyema with adequate follow-up data in which early rapid closure of the pleural cavity occurred, there were 17 in which correction of a spastic type of curvature took place soon after the establishment of the drainage, 26 in which no deviation developed and only 2 in which slight curvatures persisted after a complete cure of the empyema (table 10).

Pleural scoliosis frequently does not develop until weeks or months after the onset of the empyema, and not infrequently the curvatures progress gradually over a period of many months. Von Kölliker [23] and Hedblom [24] have observed a progression of curvatures for as long as two years. Latent progressive curvatures developed in 26 of 62 cases of chronic empyema in which adequate data were obtainable for a period of three months or more.

Operations Which Produce Imbalance of Muscle Function (Phrenicectomy, Scaleniotomy and Intercostal Neurectomy).—A study of 50 consecutive cases of pulmonary tuberculosis in adults who were treated by phrenicectomy alone failed to reveal a deviation of the spine which could be attributed to the paralysis of half the diaphragm produced by this operation. An interval of at least three months after operation elapsed between comparative observations.

Harrenstein [25] reported the occurrence of scoliosis in 2 infants with unilateral diaphragmatic paralysis resulting from injury at birth. He attributed the scoliosis to the diaphragmatic paralysis. In both cases

23. von Kölliker, T.: Zur Verhütung und Behandlung der pleuritischen und empyematischen Skoliose, Deutsche med. Wchnschr. **30**:634, 1904.

24. Hedblom, C. A.: Deformity of the Thorax Secondary to Pleural or Pulmonary Disease, J. A. M. A. **94**:162 (Jan. 18) 1930.

25. Harrenstein, R. J.: Das Entstehen von Skoliose infolge einseitiger Zwerchfellähmung, Ztschr. f. orthop. Chir. **56**:101, 1932.

there were also extensive injuries to the brachial plexus, with paralysis of all of the muscles of the arm, which offers a more likely explanation of the scoliosis.

By unilateral phrenicectomy Marconi [26] produced scoliosis in young rabbits in which rickets had been simultaneously produced experimentally by the administration of a strontium preparation. The convexity of the primary curvature was always on the paralyzed side.

In three patients treated by scaleniotomy (division of the three scalene muscles) no change occurred in the contour of the spine.

Four cases in which multiple intercostal neurectomy had been done were studied. In 3 of them slight but definite deviations of the spine developed after operation, and in each instance the convexity of the curve pointed toward the side on which operation had been performed.

Lobectomy and Drainage of Pulmonary Abscesses.—Following total extirpation of the lower lobe of a lung in 11 consecutive cases of bronchiectasis, a thoracoplasty type of scoliosis developed in 9 instances. The curvatures were slight in 3, moderate in 5 and severe in 1 case. The last case is illustrated in figure 11. In this case only was there a curvature before operation, and this curvature was slight.

Since the incidence and extent of the curvatures which develop after lobectomy are greater than reasonably could be explained by the imbalance produced by the costal resections necessary for the operative approach, it would appear that other factors contribute to the imbalance. The large space which is left after the lobe has been removed is obliterated by the remaining lobes, the mediastinum, the diaphragm and the thoracic wall, which are drawn into the space by contracting fibrous tissue. It is probable that the vertebral bodies are pulled laterally toward the thoracic wall and take part in obliterating this space.

Surgical drainage of pulmonary abscesses in 15 cases was productive of spinal deviations in only 5 cases; 4 deviations were slight, and 1 was moderate. Before operation there was a curvature (slight) in only 1 case. Drainage of the lower lobe was done in 2 of these cases; curvature of slight degree developed in 1 case and of moderate degree in the other.

Miscellaneous Thoracic Operations; Induced Pneumothorax and Extrapleural Pneumolysis.—Occasionally an artificial pneumothorax may cause the spine to deviate slightly. Since the intrapleural pressures and other circumstances related to pneumothorax therapy are so inconstant, no statistical data were collected.

Twenty-two patients who were treated by unilateral extrapleural paraffin pneumolysis were studied. Slight deviations developed in 14

26. Marconi, S.: Alterazioni rachidie sperimentali da tossici, Chir. d. org. di movimento **13**:585 (July) 1929.

of the series. The convexity of the curve was directed toward the side of operation in 10, and toward the opposite side in 4 cases.

PREVENTION AND TREATMENT OF PLEURAL SCOLIOSIS

Although the principal interest in most of the spinal deviations incident to thoracic disease and thoracic operations is academic, a certain small minority progress to a stage of deformity. The deformities occur only in certain cases of pleural scoliosis, occasionally subsequent to extensive costal resections and lobectomies, and only in children and young adults.

Extensive deformity from any cause produces not only disfigurement of great concern to the patient, but also much impairment of cardiac and respiratory functions and often subjective symptoms such as pain and ease of fatigue. The restriction of respiratory excursions greatly reduces the capacity of pulmonary ventilation. Disturbed anatomic relations of the heart and great vessels which impair their functional efficiency and evidence of interference with the return flow of the pulmonary circulation with chronic passive congestion of the lungs have been observed frequently at necropsy (Eckhardt [27]). These factors not only limit the patient's activities but also diminish his ability to combat any severe illness successfully. Pneumonia is a frequent cause of death.

As pointed out previously, the spinal deviations associated with acute nontuberculous empyema usually correct themselves when the empyema cavity is obliterated promptly. Deformities develop with the chronicity of the disease, which, with few exceptions, reflects improper treatment. The first objective in the prevention of pleural scoliosis is therefore the early closure of empyema cavities by early, adequate and dependent drainage. Von Kölliker [23] stated that the development of scoliosis is best prevented by the rapid healing of the disease. No scoliosis developed in any of his cases in which drainage was done early by rib resection.

In pure tuberculous effusions rapid closure of pleural cavities may be effected only by repeated thoracenteses, because drainage is contraindicated, but drainage is applicable to many tuberculous effusions which are secondarily infected by pyogenic micro-organisms.

In all cases with pleural effusions, regardless of the etiology, a constant effort should be made to hold the spine in alinement or slightly overcorrected during the major portion of each twenty-four hours, not only during the period of active treatment, but also for several months after the pleural cavity has been obliterated in order to prevent deform-

27. Eckhardt, H.: Untersuchungen über die Lage von Brust und Baucheingeweiden bei hochgradiger Kyphoskoliose, Ztschr. f. orthop. Chir. **48**:125, 1927.

ity from latent contracture of the pleural scar. With the exception of infants and uncooperative children, this can be accomplished in most patients by posture; the patients lie on their affected sides, and if this simple procedure does not deviate the spine in the direction of overcorrection sufficiently to counteract the tendency to a pleural scoliosis, it may be supplemented by wedging, which is described under the topic "postural wedge compression." In ambulatory patients it may be carried out during rest hours during the day and at night.

Gaugele [20] advised the use of an Abbott plaster jacket for the prevention, as well as the correction, of pleural scoliosis. The jacket is provided with a window for the care of drainage tubes and dressings. The Abbott treatment of all forms of scoliosis has in recent years been abandoned, and its use in the presence of active disease of the pleural cavity would be objectionable because of the interference with respiration and the proper supervision of the empyema, the lesion of primary importance.

As pointed out previously, the extensive costal and pleural resections of extrapleural and Schede thoracoplasties, when done primarily to obliterate chronic residual pleural cavities, may partially or completely correct mild or even deforming pleural scolioses. Not infrequently an overcorrection is produced, and this is treated as a simple thoracoplasty scoliosis.

These same principles have been utilized by Hedblom,[24] Lilienthal,[28] Sauerbruch,[29] Gurd [30] and others in the treatment of residual pleural scoliosis in patients who have been cured of pleural or pulmonary disease. These surgeons have reported marked correction of curvatures by removal of ribs and pleural scars and by pulmonary decortication.

PREVENTION AND TREATMENT OF THORACOPLASTY SCOLIOSIS

Although the vertebral column deviates or sags into the unsupported side of the chest after the extensive costal resections of a posterolateral thoracoplasty, it is sufficiently plastic to permit considerable molding and correction by force until it becomes fixed from four to eight weeks after operation by the regenerated ribs, organized fibrous tissue and reinserted muscles. If correction is maintained during this reparative period, permanent curvatures will be minimized and often prevented. If, however, the periosteum has been destroyed or excised (as it is in a Schede thoracoplasty) the resected costal segments are not replaced, and the

28. Lilienthal, H.: Thoracic Surgery, Philadelphia, W. B. Saunders Company, 1925, vol. 1.

29. Sauerbruch, F.: Chirurgie der Brustorgane, Berlin, Julius Springer, 1920, vol. 1.

30. Gurd, F. B.: Scoliosis Accompanying Chronic Infected Open Pneumothorax, Arch. Surg. **5**:366 (Sept.) 1922.

spine is permanently deprived of much of its support on the side on which operation has been performed. In many instances, however, this lack of support may compensate for the previous imbalance from the pleural scar and merely correct a preoperative pleural scoliosis. The postoperative prophylactic maintenance of correction by postural wedging in these cases is beneficial but less effective than in the cases in which extrapleural thoracoplasty is done.

COMPRESSION BY A POSTURAL WEDGE

The spine can be controlled and held in a corrected or overcorrected position most simply and most effectively by posture alone or by compression by a postural wedge. In the latter procedure, illustrated in figure 12, the patient lies on the diseased side or the side on which

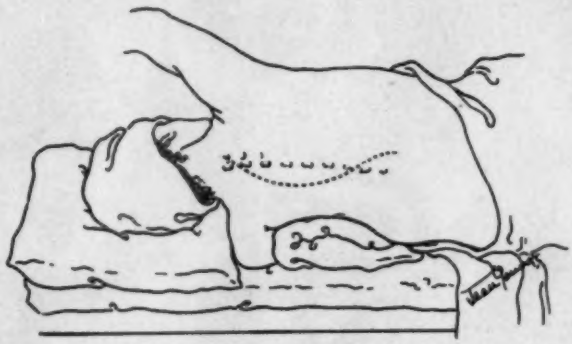

Fig. 12.—Postural wedge compression (Bisgard, J. D.: J. Thoracic Surg. **3**:99 [Oct.] 1933): The patient lies on the diseased side or the side on which operation was performed, over a pillow which has been rolled in the direction of its long axis and placed at right angles to the axis of the body. By placing this fulcrum properly, the spine can be wedged in the direction desired. To correct and prevent pleural scoliosis, the fulcrum is placed high in the axilla, wedging the spine in the direction of overcorrection. To correct a thoracoplasty scoliosis the wedge is placed slightly more distal, that is, directly opposite or slightly caudal to the apex of the curve. The change of spinal contour which can be brought about by this procedure is illustrated diagrammatically by the straight alinement of the spinous processes. The curved, broken line illustrates the position of the spine of a thoracoplasty scoliosis before wedging.

operation has been performed, on a soft compression wedge, such as a pillow which is rolled in the direction of the long axis and placed at right angles to the axis of the body. If this fulcrum is placed properly, the weight of the body wedges the spine in the direction desired. In cases of developed or potential pleural scoliosis, the wedge is placed high in the axilla of the diseased side (with the arm completely abducted and the head elevated) so that the entire thoracic spine is deviated in

the reverse direction, the direction of overcorrection. To correct and prevent thoracoplasty scoliosis, it is placed exactly opposite or slightly caudal to the apex of the curve, thus applying pressure on the spine at a lower level. The correction which can be obtained by postural wedging is illustrated in figure 13.

This procedure not only is the simplest and most effective method of controlling the vertebral column, but also has the added advantage of contributing compression and immobilization to the thoracic wall and rest to the diseased lung or pleurae. Also, it does not interfere with the free respiratory excursions and pulmonary ventilation of the

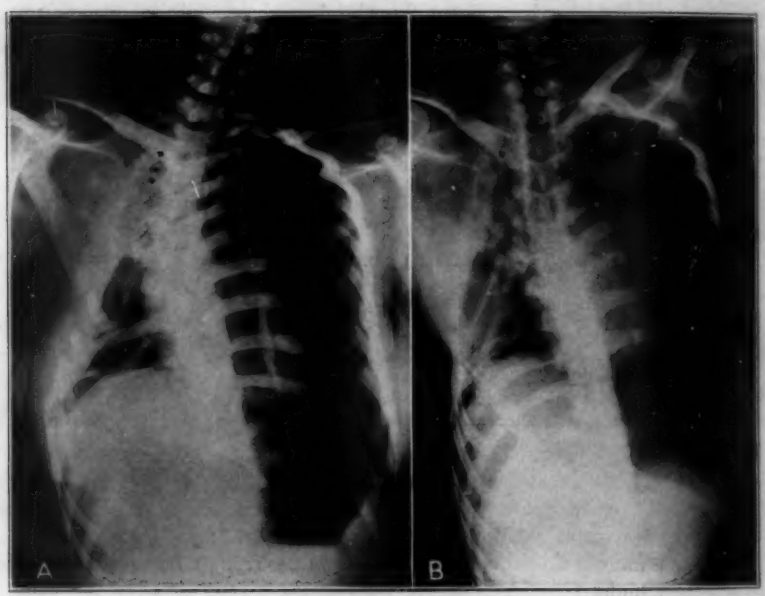

Fig. 13.—Postural wedge compression: *A*, a roentgenogram of a thoracoplasty scoliosis taken with the patient sitting upright. The first stage operation had been done three weeks, and the second stage operation one week, previously. *B*, the same patient; this roentgenogram was taken during postural wedging, with the patient lying on the side on which operation occurred. In comparing the two roentgenograms, note that almost complete correction of the curvature has been obtained by wedging. The arrows in both roentgenograms outline an open pulmonary cavity which is partially concealed by the vertebral shadows in *B*, but with the vertebrae wedged into straight alinement in *C*, its entire circumference is clearly visualized. This use of postural wedging to gain increased roentgenologic visualization of the compressed lung after thoracoplasty has been reported elsewhere (Bisgard, J. D.: J. Thoracic Surg. **3**:99 [Oct.] 1933).

healthy side. Except for these reasons the curvatures of pleural scoliosis could be wedged equally or more effectively with the patient lying on the unaffected side, with the fulcrum placed at the apex of the curve.

To illustrate this point and to indicate other circumstances in which postural wedging may be used, a case is cited.

Recently a child with extensive third degree burns of the left half of the trunk was treated by postural wedging. As a result of protective spasm and scar contracture, a moderately severe dexter convex curvature had developed. The curvature was promptly corrected with the patient lying on the uninvolved side over a rolled pillow, and the correction was constantly maintained until the burned areas had become completely epithelized with the aid of skin grafting. The child was examined one month after weight bearing had been resumed, and the spine was straight.

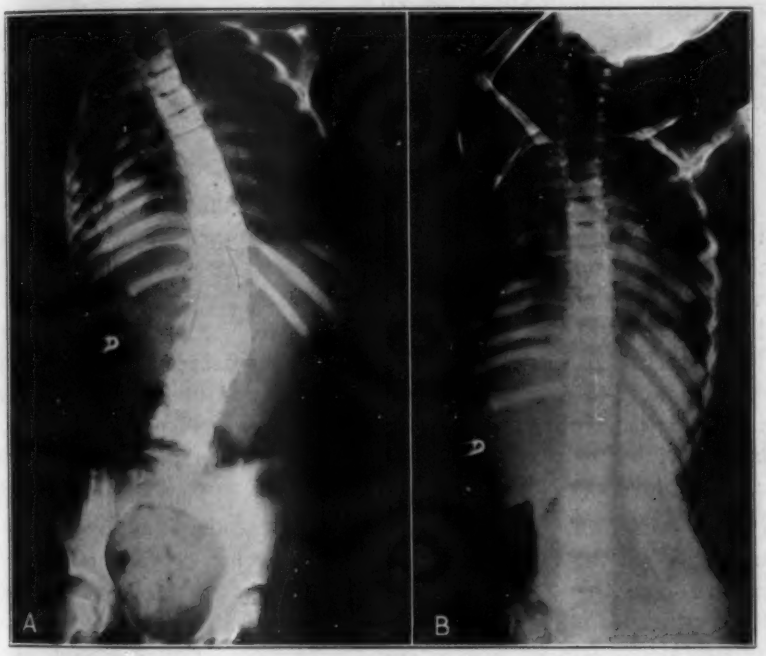

Fig. 14.—A child of 7 years with chronic empyema and an early pleural scoliosis: *A*, roentgenogram taken with the patient standing, and *B*, roentgenogram taken with the patient lying and undergoing postural wedging.

Young children may be held in position for postural wedging in a plaster bed which is molded to the body with the patient lying on the side. The side walls should be high enough to prevent the child from rolling out of this position.

With cooperation from the patient, postural wedge compression may be started immediately or a day or two after operation and within a few days may be maintained almost continuously.

For a few cases in which well developed deformities occur and for cases in which the curvatures are definitely progressing, the following

procedures have been recommended by many orthopedic surgeons: (1) corrective gymnastic and breathing exercises; (2) supportive body braces and jackets; (3) longitudinal traction on the head and pelvis, and (4) osteosynthesis of the spine after correction with a Risser turnbuckle cast.

When established, the curvatures of pleural and thoracoplasty scolioses are more resistant to correction than all other types, such as the paralytic and the idiopathic. When they are progressive, their progression likewise is much more difficult to prevent and usually continues despite the support of a body jacket or brace. Likewise, stretching and corrective exercises neither correct nor alter the course of progressive scoliosis. In most instances these curvatures can be controlled only by the internal fixation obtained by fusion of the entire spinal segment which constitutes the primary curve.

SUMMARY

1. A study of the influence on the spinal column of thoracic disease in 518 cases and of the surgical operative treatment of thoracic disease in 336 cases is reported. While lateral deviations of the thoracic spine had developed in a large percentage of cases in both groups in only 11 cases were the deviations great enough to give rise to a deformity of major clinical importance. Deforming curvatures occurred in only a few cases with extensive chronic pleuritis and in an occasional case in which successful treatment necessitated an extensive Schede thoracoplasty or lobectomy. It is significant that these deformities occurred only in children and young adults (less than 20 years of age).

2. Certain observations and deductions of academic interest are presented. With the etiology of many thoracogenic curvatures definitely known and capable of analysis, an unusual opportunity is given to study the mechanics of the thoracic spine. The various types of curvatures and the mechanism by which they are produced are described. This mechanism is presented on the basis of an imbalance of the opposing forces acting on the vertebrae.

3. All curvatures may be divided into two principal groups: (*a*) Rotary scoliosis. In thoracoplasty, as in most, if not all, types of scoliosis with the exception of pleural scolioses, the force of torsion associated with lateral deviation causes the vertebral bodies to rotate into the side of convexity. (*b*) Nonrotary or pleural scoliosis. All curvatures produced by the scar of chronic pleuritis are designated as pleural scolioses. This type of curvature is unique in respect to the absence of rotation of the vertebral bodies.

4. Methods of prevention and treatment of thoracogenic curvatures are discussed. Most pleural scolioses may be prevented by the early cure

of the pleural disease and by constant maintenance of correction or overcorrection of the spine by postural wedging. Also, many instances of thoracoplasty scolioses may be prevented by constantly wedging the spine straight until it becomes fixed.

For the control and treatment of certain severe and progressive curvatures, internal fixation by fusion of the vertebral column is recommended. Every patient less than 20 years of age who has had chronic infection of the pleural cavity or has been treated by extensive thoracoplastic operations should be observed frequently for at least a year, and if the curvature shows a tendency to progress despite conservative treatment, the spine should be fused to prevent the development of a severe deformity.

From this study and from clinical observations the author has been unable to discern any criterion by which one may prognosticate in an individual case the likelihood or degree of development of thoracogenic curvatures.

HEALING OF FRACTURES

ITS INFLUENCE ON THE CHOICE OF METHODS OF TREATMENT

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For the last two decades the problem of bone formation in its various aspects has occupied the attention of many investigators. That phase of the question which deals with the mechanism of healing after fracture has been prominent in the field, and during this time quite new conceptions of the process have been evolved. From the purely academic aspect many points relative to the exact mechanism of the process are disputed. It may be considered that there is no unanimity of opinion on the following questions: (1) whether there exist in the human adult specific bone-forming cells—osteoblasts; (2) whether such cells can be evolved on demand, so to speak, by metaplasia of ordinary fibrillar connective tissue cells; (3) whether only certain connective tissue cells are capable of this transformation; (4) whether the cell itself plays any active part of a specific nature in the process; (5) whether there is formed in the process of ossification a specific preosseous substance or matrix, and if so, (6) whether, after it is calcified, it is possible to remove calcium therefrom without coincidentally removing the associated matrix; (7) whether the deposition of calcium in the tissue associated with the formation of bone, be it in a preosseous matrix or not, is the result of the activity of an enzyme or independent of it; (8) if an enzyme is involved, whether it is the product of local cellular activity, specific or otherwise, or of local death of cells, or whether it originates at some point remote from the site of the formation of bone and is brought to the scene of action by the blood stream. The bibliography covers the range of the investigations along these lines and reveals a tremendous diversity of opinion.

Disregarding for the purposes of this article the purely academic side of the question, and taking into consideration only the phases of the problem which can be of practical working value to the man who has to take care of fractures and promote their prompt and efficient healing, there can be gathered from the mass of conflicting findings and inter-

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From the Fracture Service of the Presbyterian Hospital and the Department of Surgery, College of Physicians and Surgeons.

Read before the Section on Orthopedic Surgery, at the Eighty-Fourth Annual Session of the American Medical Association, Milwaukee, June 16, 1933.

pretations thereof a number of observations which appear to have sufficiently substantial support to warrant clinical application in the treatment of fractures in the adult.

I shall first present the observations which are sufficiently well supported to be, if possible, clinically applied; next, a résumé of the main supportive evidence for these observations, and finally, my point of view as to the influence of these observations on the treatment of fractures in general and as to the special application of some of them to specific fractures.

A. OBSERVATIONS SUFFICIENTLY WELL SUPPORTED TO BE, IF POSSIBLE, CLINICALLY APPLIED

I. All fractures heal as do wounds elsewhere, unless there is a mechanical, chemical or anatomic bar to the healing. This healing, in common with that of wounds of the soft parts, takes place through the medium of new connective tissue known as granulation tissue. When referring to delayed union and nonunion after any fractures in which healing through granulation tissue has occurred, one in reality refers to a delay or failure in the process of calcium deposition in the healing connective tissue which is commonly designated as new bone formation.

II. Variations in the character and amount of the healing process in bone following fracture are dependent on factors limited to the region of the body involved, quite independent of the subject involved.

Corollary 1.—Slow union and nonunion are not influenced by the age (per se) of the patient, by his general state of health, by the presence of chronic general disease such as syphilis or cardiovascular or renal disease, by general wasting due to other causes, by general metabolic disturbances affecting either the general calcium and phosphorus metabolism (osteomalacia) or other phases of metabolism (diabetes) or by acute infectious disease.

Corollary 2.—Therapy designed to alter the patient's general metabolism, specifically to affect his general calcium or phosphorus metabolism or his general state of health, have no appreciable effect on the process of healing.

III. The four factors involved in the mechanism of the healing of fractures and capable of being clinically influenced are: (1) the local pathology; (2) the growth of granulation tissue; (3) an available local source of calcium for the ossification of the healing tissue, and (4) a proper biochemical status of the local tissue fluids throughout the healing process.

Local Pathology.—The items of importance under this factor are: (*a*) The amount of tissue necrosis. When massive, it destroys available sources for the growth of granulation tissue and under all circum-

stances it creates a p_H to the acid side (often markedly so) in the hematoma and tissue fluids about the site of the fracture. This p_H is of importance in the production of the local source of calcium and is the essential early stage of the biochemistry of the tissue fluid.

(*b*) The hematoma or blood effusion at and about the site of the fracture. This influences the growth of granulation tissue through its fibrin content and the possible persistence of its fluid content in situ, and also the establishment of a local source of calcium under proper conditions of p_H in the tissue fluid by acting essentially as a decalcifying fluid and, through adsorption affinity between calcium and its fibrin content, by holding the freed calcium in situ.

(*c*) The circulatory status of the part (including the lymphatic and tissue fluids) in the early and late stages of fracture healing. Its significance lies in its influence on the growth of granulation tissue, and on the establishment of and utilization of a local source of calcium through its influence on the p_H of the tissue fluids.

(*d*) Chemical and physical influences through their effect on the growth of granulation tissue and the biochemical status of the part. Under the former may be noted the therapeutic use of chemicals locally (disinfectants, etc.) and infection, and under the latter, the use of such agencies as roentgen rays and diathermy.

(*e*) The mechanical element, i. e., the interposition of living or dead material impermeable to the growth of granulation tissue between the fragments.

Growth of Granulation Tissue.—The items of importance under this factor are: (*a*) The amount of tissue necrosis in relation to the amount of healing tissue called for in replacement. All other factors being equal, the amount of callus produced is directly proportional to the amount of granulation tissue produced.

(*b*) The amount of tissue necrosis in its relation to the destruction of available sources for the growth of granulation tissue.

(*c*) The anatomic characteristics of the part in relation to the availability of sources for the growth of granulation tissue and accessory circulation.

(*d*) The amount of fluid persisting for a long period at the site of the fracture.

(*e*) Elements *d* and *e* mentioned under local pathology (chemical and physical influences and the mechanical element).

Available Local Source of Calcium.—The items of importance in the ossification of the healing tissues are: (*a*) The amount of bone necrosis.

(*b*) The density and degree of fragmentation of the necrotic bone.

(*c*) The influence of fibrin and collagen in fixing the calcium locally through chemical affinity.

(*d*) The biochemical status of the local tissue fluids.

Proper Biochemical Status of the Local Tissue Fluids Throughout the Healing Process.—This factor involves the necessity in the local tissue fluid of a p_H on the acid side in the early days following the fracture in connection with the establishment of a local source of available calcium for ossification of the healing tissue, and a reversion of the p_H of the local tissue fluid toward the alkaline side before the calcium made available can be to any extent deposited in the new tissue to form bone. The constituents normally involved in this phase of the process are the amount of tissue necrosis, the content of local living tissue cells, the degree of metabolic activity of the cells and the circulatory status (blood and lymph) of the part.

B. EVIDENCE SUPPORTING THE OBSERVATIONS LISTED UNDER A

I. Whether, as an academic question, there exists in the adult a specific osteoblast essential to new bone formation, whether any or certain connective tissue cells may under proper conditions be transformed through metaplasia into cells specifically concerned in new bone formation, i. e., become osteoblasts, or whether there is no need for the specific activity of any cell in the process—new or young connective tissue being the only necessity—it must be acknowledged that the actual formation of bone occurs only after undifferentiated connective tissue healing and by a transformation of that healing known as ossification. Regardless again of the academic discussion as to whether this transformation is effected with or without the formation of a preosseous matrix and as to whether the calcium deposition therein is the result of the activity of a ferment or independent of such an activity, it is to the transformation of ordinary wound healing into bone that the terms slow union, delayed union and nonunion refer. The only true nonunions—that is to say failures of healing—are those due to the mechanical, chemical, physical and anatomic causes discussed subsequently under III (factors involved in the healing of fractures).

II. The preponderance of evidence, clinical and experimental, supports this observation. In the absence of the local factors mentioned under I of section A and discussed under III of this section, which prevent even ordinary connective tissue healing, and interpreting the terms slow union, delayed union and nonunion to refer to variations in calcium deposition in the healing connective tissue, the following may be listed in support of observation II and its corollaries:

Certain regions of the body, even under apparently optimum conditions, are characterized by a slow average healing time and by fre-

quent occurrence of delayed union and nonunion in adults. The neck of the femur (subcapital or midcervical), the junction of the lower and middle thirds of the tibia, the scaphoid of the carpus (proximal half), the base of the fifth metatarsal and the junction of the lower and middle thirds of the humerus are characteristic regions.

In patients who have fractures in these regions and simultaneous fractures in regions not so characterized there is no perversion of healing in the latter, all other factors except location being equal.

The preponderance of evidence based on recorded observation and not on impression is against the influence of any of the factors listed under corollary 1. All the factors listed may influence mortality markedly. In a leg which has been edematous and secondarily fibrosed for a long time as a result of cardiac or renal disease the healing may be abnormally slow, but the cause is the local circulatory status and not the cardiac or renal disease. If the local circulatory status can be influenced, even by mechanical means, healing may be influenced, though the disease itself may go on to a fatal issue while the healing is progressing normally. Similarly it is true that older people are more subject to vascular and chronic cardiac or renal disease. The mortality is apt to be high following injury in these patients. But if the local circulatory status of the part involved by fracture is not irreparably compromised, the healing of a fracture is not affected, nor is it at all affected in a patient of any age if there is no impairment of the circulatory efficiency of the part.

The theory that the presence of syphilis is deterrent to the healing of a fracture has long been exploded. It is conceivable and probable that local vascular impairment, local necrosis and sclerosis of the bone from any cause may be factors interfering with the normal process.

The preponderance of clinical and experimental evidence on the calcium and phosphorus levels of the blood during the healing of a fracture is unquestionably to the effect that there is no correlation between variations in these levels and variations in the healing process. In keeping with this are the clinical findings in osteomalacia and rachitis, in which healing is normal or slightly more rapid than normal after fracture, although there exists an actual negative balance in the former and an acknowledged metabolic disturbance in the latter. In cases of fragilitas ossium the healing is also unaffected by the presence of the disease. The same is true of cases of fibrocystic disease per se. A case at the Presbyterian Hospital a few years ago furnished a striking example of the lack of correlation between the state of calcium metabolism and the healing of a fracture. A gastro-enterostomy had been performed four years previously for the relief of a supposed gastric ulcer. The patient was admitted several times for successive spontaneous fractures. Roentgen examination showed general osteoporosis.

The phosphorus and calcium levels of the blood remained constantly normal, though the patient showed a negative balance. Eventually death resulted from an embolus. An autopsy showed the supposed gastro-enterostomy to have been a triple anastomosis between the stomach, jejunum and transverse colon as the result of a gastrocolic fistula, so that most of the food passed directly from the stomach to the transverse colon. Under these conditions the intake of calcium was negligible, and the blood calcium was kept up by withdrawals from the skeletal system. Despite this situation all the fractures healed with profuse callus.

My personal observations and the recorded clinical observations of others offer no support for the suggestion that there is any material variation in the healing of a fracture in patients with general metabolic disturbances, such as diabetes, disease of the thyroid gland and similar conditions, which is referable to the disease in the absence of thoroughly adequate grounds for such variation at the site of the fracture.

Corollary 2 follows 1 as a logical sequence, and, in addition, is supported by the recorded literature and by my personal investigations and observations over a number of years.

III. The following factors are involved in the mechanism of fracture healing:

1. *Local Pathology.*—(*a*) Tissue necrosis. The primary healing following a fracture is always by a tissue indistinguishable from granulation tissue; this tissue can be, and often is, derived in large part from tissue entirely outside of the bony structures; in fact, following tissue necrosis in the soft parts quite distant from bone, the formation of bone occurs in numerous sites in the body following disease and injury and can be produced experimentally in granulation tissue without the introduction of any osseous elements. Massive necrosis of tissue affecting the sources for the growth of granulation tissue into and about the site of the fracture from osseous or soft part structures is obviously a bar to the primary healing, without which the subsequent healing of the bone is impossible. Necrosis of tissue is accompanied by autolysis and often by a marked change in p_H to the acid side in the tissue fluids. A p_H as low as 4.2 has been recorded. The local primary acidity over a period of days (for which tissue necrosis is partly responsible) has been definitely established after a fracture. The importance of this primary acidity of the tissue fluids and its rôle in the decalcification of the dead bone at the site of the fracture is discussed in more detail under factors 3 and 4.

(*b*) Hematoma or blood effusion at the site of the fracture. By animal experiment and observations on tissue cultures, the relationship between adequate formation of fibrin network and satisfactory growth of granulation tissue is made clear. The demonstrated early acid p_H

of the fluid portion of the blood effusion is of significance as regards its effect on the p_H of tissue fluid and its rôle in making local calcium available and in utilizing it for deposition, as is the chemical affinity of fibrin for calcium (similar to that existing between calcium and the hyalin of hyaline cartilage and the collagen in which new connective tissue is so rich), which can serve to hold locally available the calcium liberated from dead bone at the site of the fracture. During the days just following the fracture the fluid portion of the hematoma is a factor of importance through its p_H in establishing the local source of calcium; if it is extensive and remains as fluid in situ (dependent on local circulatory efficiency), it may be a hindrance to the proper progress of the growth of granulation tissue (the effect of a fluid medium on the growth of tissue). The reputed backwardness in the healing of fractures bathed in synovial fluid is thus logically explained.

(*c*) The circulatory status of the part, including the tissue fluids, in early and late stages of fracture healing. The evidence supports the view that for the first week or so following a fracture there is normally a p_H definitely and often markedly to the acid side, dependent on elements cited under "local pathology" and under "biochemical status of the tissue fluids." The necessity for this acid p_H is discussed under 4. Relative circulatory stasis in the part is essential at this time to render available for use calcium derived from dead bone at the site of the fracture, decalcification of such bone occurring only in an acid medium. The circulatory stasis prevents the too rapid carrying off of the acid products of necrosis and autolysis which are largely responsible for the p_H status, and actually intensifies this status by its effect on the metabolism of the living cells present. The analogy may be aptly drawn between the status of the part as regards the p_H of tissue fluids and the carbon dioxide concentration in a given room. The parallel involves four main factors: (1) the number of people in the room, corresponding to the cell population in a given region of tissue; (2) the state of metabolic activity of those people—active, quiescent or in a state of death and dissolution—the parallel in the tissues is obvious; (3) the chemical characteristics of the air supplied to the room, corresponding to the qualitative circulatory status of a given part; (4) the rate of renewal of the air supplied to the room, corresponding to the quantitative circulatory status of a given part.

Similarly, following this initial period of stasis, a return to the normal circulatory status will be accompanied by a diminution in the acidity of tissue fluids, to a point compatible with the deposition of the freed calcium. This apparently occurs only in the presence of the more alkaline p_H (this holds true under all points of view advanced in the academic study of the exact mechanism of this deposition); when the fluid content of the hematoma is large and it has remained localized

and undiffused its diminution through the increased circulatory efficiency removes a definite bar to the growth of tissue.

Impairment of the circulatory status sufficient to cause massive necrosis is discussed under 1(*a*). The result of prolonged circulatory stasis with its effect on tissue metabolism and its maintenance of acidity in the p_H of tissue fluids is obvious. It is also obvious that when the amount of necrosis is extensive but not sufficiently massive to obviate the possibility of adequate growth of granulation tissue in replacement, the time needed to restore the p_H of tissue fluids to levels compatible with calcium deposition is in direct proportion to the interrelationship of two factors: the amount of necrosis and the speed of restoration of circulatory efficiency. In patients with a small amount of necrosis and with a normally rich circulatory apparatus the element of rapid restoration of a high degree of circulatory efficiency becomes a matter of relatively little importance in the treatment as regards the healing of bone. Proportionately to the increase in the amount of necrosis and the anatomic capabilities of the part as regards circulatory efficiency, this element becomes more and more important in the treatment from the standpoint of calcium deposition, viz., healing of bone.

(*d*) Chemical and physical bars to the healing of tissue. The influence of infection in producing continuous necrosis by chemical means, thus preventing primary healing, is obvious, and it has been demonstrated that with many suppurative processes there is established, even in the absence of extensive necrosis, an acid p_H resulting in the decalcification of bone and in but little or no calcium deposition in the granulation tissue which may, however, be overabundant. Unfortunately I am not aware of any investigation of the interesting question of the p_H of tissue fluid in low grade and relatively chronic infections characterized by increased formation of bone or exuberant callus after fracture. Included in the group of physical influences I should like to mention the effect of diathermy (considered as internally applied heat) and of roentgen rays. Diathermy under high milliamperage, as frequently used early in the treatment of fractures, may be, and unquestionably frequently is, a definite bar to healing by an actual devitalization of the tissue, aiding decalcification but interfering with the subsequent calcium deposition (factor 4). Its beneficial effect under any circumstances in this respect is highly problematic; if there is any, it can be exercised only at low milliamperages producing no damage to the tissues and can be of benefit only in relaxing vascular spasm to relieve congestion. It is highly improbable that after the first five to seven days constant local circulatory congestion can have any except a deterrent effect on calcium deposition. Exposure to roentgen rays is subject to the same general reservations.

(*e*) Mechanical bars to the growth of tissue. The rôle played by soft parts, including periosteal flaps, whether living or dead, and by large fragments of dense bone, if dead, as mechanical bars when interposed between the ends of the bone requires no discussion.

2. *Growth of Granulation Tissue.*—(*a*) This point is supported beyond dispute by clinical (including roentgenographic) and experimental evidence and holds true up to the point of massive necrosis as discussed under *b*.

(*b*) When necrosis becomes sufficiently massive it serves obviously as a bar to the growth of granulation tissue through the removal of all locally available sources for such growth.

(*c*) The anatomic characteristics of the part are frequently a reason for the lack of growth of granulation tissue. When a fracture occurs in a region such as the neck (intracapsular) of the femur or the proximal half of the carpal scaphoid there is naturally a varying amount of necrosis and circulatory damage. Because of the exceedingly minimal or even totally lacking circulatory status of the proximal bony fragment in each instance the source for the growth of granulation tissue and adequate accessory circulatory supply is in the surrounding soft parts. In the former case there is only the dense fibrous capsule; in the latter there is frequently nothing at all, or, at most, a mere bit of fibrous ligament. Thus scant growth of tissue occurs, often with so-called "aseptic" necrosis of the separated portion of bone. Even if some growth of granulation tissue is possible, it is hindered by the presence of synovial fluid (the effect of a fluid medium on the growth of tissue). In contrast to the femoral neck with its characteristic changes even when adequately reduced, one notes the intertrochanteric region but a few centimeters away, where, in a class of patients identical with those in the group with a fractured neck, the healing by bony union is not only profuse and rapid but occurs so universally that these fractures heal despite obvious gross mistreatment and under practically all conditions. The essential difference lies in the fact that the intertrochanteric region is buried in large fleshy and vascular muscular attachments—a rich accessory circulatory reservoir. The fluid may be a factor in all fractures involving joints sufficiently to allow the bathing of the fractured surfaces in synovial fluid. The factor of a deficient source for new tissue holds true in explanation (so far as the growth of tissue is concerned) of fractures at the junction of the lower and middle thirds of the tibia and similarly characteristic regions, where the soft parts surrounding the bone are largely skin, tendon and fascia providing a poor source of growth. The site in the tibia is particularly interesting from this standpoint since the inner face with a tightly overlying skin affords the scantiest growth of tissue and resultant healing

of bone; the external face, with its tendinous and areolar planes, affords but little more, and the posterior face, with its muscular attachments, shows the greatest amount of callus. The analogy to the neck of the femur and intertrochanteric region is obvious.

(*d*) The amount of fluid persisting over a long period at the site of the fracture offers a definite bar to the adequate growth of granulation tissue. A large hematoma which remains circumscribed and synovial fluid are good examples. It is to be remembered in the former case, however, that hematoma fluid has been shown after a number of days to contain a large percentage of calcium from the decalcified dead bone, and any efforts to get rid of it are therefore best made before such decalcification takes place, viz., at the onset of treatment. Late removal of such fluid, while it is an aid to the growth of tissue, withdraws some of the local calcium available for deposition in the new tissue.

(*e*) The elements *d* and *e* discussed under "Local Pathology" (clinical, physical and mechanical bars to tissue growth). The influence in this connection of the factors there discussed is obvious.

3. *Source of Local Calcium.*—Not only does the clinical evidence support the view that the effective source of the calcium used for callus in the primary healing process following fracture is the traumatized bone at the site of the fracture, but experimental evidence bears out the clinical findings and in the main adequately supports the view that the levels for blood calcium and phosphorus and the general calcium metabolism have no appreciable bearing on the question of primary healing of fractures and that as a source of calcium the dead bone at the site of the fracture can actually be substituted for by calcium salts of various types introduced in replacement of such dead bone or used as a source of calcium in soft parts unconnected with bone to produce actual ossification when the other factors involved in the process of the formation of new bone are concurrently reproduced. It must be remembered that the local source of calcium is only one in a complicated interrelationship of factors, and that, while there is evidence to show that it can be substituted for, the clinical application can be considered to be purely in an experimental stage and unpractical for use at the present time.

The local decalcification of dead bone, the rapid local concentration of calcium in the soft parts surrounding the site of the fracture, the independence of these two factors from variations, clinical and experimental, in calcium intake, output and balance are all supported by the major weight of published evidence and by personal observations.

(*a*) If the source of the calcium utilized in the ossification of the healing tissue following fracture is derived locally by decalcification of dead bone, the influence of the amount of necrosis in the bone is obvious.

(*b*) If, however, this dead bone is one large mass of dense cortical bone the actual amount of calcium made available is relatively small as compared with a similar aggregate of bone in the form of small comminuted fragments or of cancellous bone. It is merely a question of surface area exposed to the decalcifying action and of feasibility of ingrowth of the tissue. It is for this reason that in general chip grafts and thin osteoperiosteal grafts or shavings result in more profuse formation of bone than do massive cortical grafts, and that a massive graft which includes both the cortex and the underlying cancellous bone is more efficient than one which comprises merely the dense cortex.

(*c*) The influence of fibrin from the effused blood and of the collagen in which young connective tissue is so rich is a matter of importance in holding in situ the calcium made available under the conditions of factor 4. The adsorption affinity between calcium and these two substances is definite and is the explanation of why the calcium remains available locally instead of being rapidly carried away as soon as circulatory efficiency approaches the normal.

(*d*) The biochemical status of the tissue fluids is a vital influence.

4. *Biochemical Status of the Local Tissue Fluids.*—Regardless of the exact mechanism whereby decalcification of dead bone occurs to furnish available calcium and of the exact mechanism whereby such available calcium is deposited in the newly formed connective tissue to form bone, all the evidence supports the view that for the former there must exist an acid p_H in the local tissue fluid, and that such a p_H is incompatible with the deposition of calcium in the newly formed tissue, the latter process being possible only when the p_H has reverted to an approximation of the normal average p_H in tissue fluid, viz., relative (as compared with the stage of tissue death and autolysis) alkalinity. The parts played in the production of these two phases of p_H in tissue fluid by the factors of tissue death from whatever cause, rate of local cell metabolic activity, local cellular richness, anatomic characteristics of the part, qualitative and quantitative status of the local circulatory process (including lymphatic and tissue fluids) and infection, have already been indicated. It is also obvious that if the biochemical status of the part is unfavorable, calcium, even if present in dead bone, cannot be made available, or if made available cannot be utilized without a change in the condition of p_H responsible for making it available.

C. INFLUENCE OF THE STATED OBSERVATIONS ON THE TREATMENT OF FRACTURES

On the basis of these observations the process of healing in a fracture is one in which, following the injury and the resultant inflammatory process, an acid p_H of the local tissue fluids, dependent on the interrela-

tionship of tissue necrosis and circulatory efficiency, is associated with decalcification of the dead bone at the site of the fracture. Such liberated calcium is held locally by a chemical adsorption affinity between it and the fibrin of the hematoma and the collagen of the newly formed connective tissue—i. e., granulation tissue—growing from all directions along the fibrin network at the site of the injury, producing a local concentration of calcium about the fracture. With increasing cell metabolism, and with interrelated increasing efficiency of circulation and carrying away of the products of necrosis, there is a reversion of this acid p_H to the alkaline side, and coincident with this change there occurs a deposition of the local adsorbed calcium in the newly formed connective tissue to form new bone. Evidence has been listed to support this point of view. If it is correct, methods of treatment can help the healing by aiding, if necessary:

(*a*) The establishment of the early acid p_H in local tissue fluids at the site of the fracture.

(*b*) The adequate growth of granulation tissue.

(*c*) The reversion at an early date to a relatively alkaline p_H in the local tissue fluids which will allow calcium deposition in the newly formed tissue.

(*d*) The maintenance of a proper interrelationship between the local metabolic activity and the circulatory efficiency.

There is no difficulty in establishing an early acid p_H. The chief danger lies in such extensive tissue death and relative circulatory inefficiency that this primary state may persist long beyond its useful stage and become a hindrance by subsequently interfering with calcium deposition. It may be considered practically impossible to restore circulatory efficiency and the coincident increased cellular metabolism with removal of products of necrosis so rapidly as to interfere with the adequate operation of tissue fluid p_H on the acid side.

In fresh fractures the local source of calcium is therefore readily established. It is extremely doubtful whether the introduction artificially of a local source of calcium in fresh uncomplicated fractures is ever necessary. If such an introduction is ever made clinically useful it will be in cases in which there is a definite loss of substance with a deficit of bone—i. e., of local calcium—or in old cases of delayed union and nonunion, in which the primary stage has been passed and a markedly avascular and noncalcified tissue occupies the region of the fracture, and then only when, coincident with the introduction of the source of calcium, the other factors involved can be established, as is the case when the operation of bone grafting is done successfully. Attention has previously been invited to the operation of this factor in the amount of bone production following various types of bone grafts.

The adequate growth of granulation tissue is dependent on an adequate source for such growth, viz., available vascularly active tissue, and the absence of deterrent agents such as excess fluid, infection and mechanical factors.

Failure of growth of granulation tissue is a frequent cause of inadequate callus. In general, one can say that the restoration of the circulatory status of the part to that approximating normal for the patient as early and as fully as possible should be the aim of treatment designed to influence this factor. The most effective means of doing so is the active use, within pain limits, of the muscular apparatus of the part from the beginning of the treatment. Proportionately as the chosen method departs from this ideal one adversely influences the growth of granulation tissue as well as the biochemical element. Active and painless muscular contraction produced by artificial (electrical stimulation) means is a relatively inefficient substitute. If this is impossible, painless gentle massage (early) may at least relax muscular and vascular spasm sufficiently to improve the local circulation. Absolute immobility of the part as a whole is least apt to aid adequate granulation tissue healing. Moreover, in cases in which the source of granulation tissue is deficient because of the anatomic characteristics of the part, as heretofore described, operative intervention—under proper circumstances as regards organization, personnel, equipment and patient—may well be indicated as the primary procedure, if, as a result of operation, not only good position but also new sources of growth of granulation tissue are obtained and early active muscular activity is made possible by rigidity of fixation at operation. In general, it can be said that healing is slower following operative care in fresh fractures than after closed treatment, except when active motion of the part is possible shortly after operation, assuming, of course, that the operative procedure is or can be so performed that extensive tissue necrosis and vascular damage are not concomitants. This is a matter for consideration in fractures in the regions referred to previously where the anatomic characteristics of the part are a bar to healing. Incidentally, as a corollary, no operative reduction should be performed under any conditions, except as a matter of necessity, unless the method of operative fixation allows early active function (if necessary through the aid of balanced suspension to relieve strain). External fixation of the part as a whole following operation is, I am convinced, commonly followed by delay in adequate callus formation for the reasons stated. Obviously, also, this has no bearing when operative reduction is a matter of necessity (in interposition of tissue, in inability to reduce otherwise, etc.), the purpose of the operation then being reduction, and it may be impossible to accomplish more than to secure a satisfactory position.

The influence of local collections of fluid on adequate growth of granulation tissue is effective in fractures of the joints through the presence of synovial fluid, and it is not evident how this factor can be obviated. On the other hand, when the accumulated and persistent collection of fluid is from hematoma, early circulatory efficiency aids in diminishing it and can be greatly helped, when the effusion of blood is obviously great, by aspiration. This aspiration should be done early, for when it is delayed the fluid contains a large amount of calcium, which is necessarily removed with it. It is also obvious that violent and repeated attempts at reduction by increasing the amount of necrosis destroy sources of granulation tissue and that operative technic must be of the gentlest and most "tissue economical" type to avoid such a result.

It is also true that, since the interrelationship of necrosis, circulatory efficiency and local cell metabolic activity determines the biochemical status of the local tissue fluids throughout the healing process, the statements made as to the possible bearing of treatment on adequate growth of granulation tissue apply equally to the question of the proper biochemical status of p_H in tissue fluids. The use of diathermy in high milliamperage and the practice of frequent or prolonged exposures to roentgen rays may interfere seriously with the healing of fractures. The use of antiseptic solutions of acid reaction in compound fractures interferes with healing. This is often clinically true of the use of surgical solution of chlorinated soda which is not carefully titrated and freshly made, which is frequently accompanied by actual decalcification of bone and slow healing. Lastly, the administration or use of agents designed to affect the general body metabolism or to affect specifically the calcium and phosphorus metabolism is without appreciable value in the treatment of fractures.

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ABSTRACT OF DISCUSSION

DR. F. J. GAENSLEN, Milwaukee: My experience with the introduction of a calcium depot in the form of calcium phosphate and calcium carbonate at the site of nonunion or delayed union is limited. In one of the cases of nonunion I drilled holes through the ends of the bone, following Boehler's technic, and then injected calcium phosphate and calcium carbonate in the form of a paste into these holes, but this proved unsuccessful. I know of at least one case in which infection followed the use of such a powder, and I am perfectly willing to let the pioneers in this work pave the way a bit farther. While I can, therefore, add nothing to this phase of the subject from clinical experience, I should like to ask a few questions.

Schanz and others have found that a high osteotomy as a palliative procedure for ununited fracture of the neck of the femur frequently resulted in bony union. This procedure does away with the shearing or wearing away effect on the neck

of the femur and establishes weight bearing on the fractured ends in a line practically perpendicular to the line of the fracture. I saw one of these cases in Boehler's clinic in 1929 one year after a high Schanz osteotomy and two years after the original injury. Bony union had resulted, and the patient walked with only a moderate limp and no pain. This was the first case which I had the opportunity of observing in which late union occurred. Later, while visiting Schanz in Dresden, I described this case to him, and he informed me that in these cases late union is not at all unusual. In a series of twelve cases which Camitz recently reported late union occurred in five, while in another of recent date the results appeared favorable. Thus, in this series of twelve cases, practically half went on to late union. Nonunion is generally attributed to insufficient blood supply, but in these cases the osteotomy in no way interfered with the actual site of the fracture, so that one must find some other explanation for success in this group.

Many years ago Hugh Owen Thomas advised percussion and damming at the site of the delayed union. Rubber constriction bands were placed above and below; the site of the fracture, protected with a felt pad, was then hit repeatedly with a wooden mallet. This was successful in many instances. I should like to hear Dr. Murray discuss these clinical observations in the light of his recent work.

Dr. Clay Ray Murray: The difficulty of clearly presenting so complex a subject in a short time is great. One must not consider the local source of calcium alone as the essential factor in healing. It is only one in a complicated interrelationship of factors. The four factors involved are: tissue necrosis, growth of granulation tissue, the local source of calcium and the biochemical status of the local tissue fluids, dependent in part on the interrelationship between tissue necrosis and vascular efficiency.

From the standpoint of these four factors an analogy exists between the intertrochanteric region and the radial site used in my experimental work and the neck of the femur and the ulnar site used by Dr. Key. The radius is covered by vascular muscular attachments, as in the intertrochanteric region, and the ulna is subcutaneous—analogous to the vascularly poor soft parts about the femoral neck; this is an important factor.

Dr. Compere quotes work on the carpal bones. They rate with the tibia and ulna. Regardless of the calcium element the vascular factor results in nonunion.

An analysis of experimental results must include a consideration of all four factors and not only of the local source of calcium.

In the nineteenth edition of Lexer's "Allgemeine Chirurgie" the vascular situation during fracture healing is illustrated by injection into experimental animals. This demonstration definitely shows that the increased vascularity occurring after fracture is almost entirely in the periosteum and the surrounding soft parts.

Stirling in Edinburgh and Rollo in Italy have both secured healing in bone gaps (radius) employing solutions of calcium instead of the powder as I did.

As to the influence of the periosteum on osteogenesis except as a transmitter of circulation from the soft parts, Bancroft in 1912 removed all of the periosteum and endosteum possible and obtained a solid union with chip grafts.

There is a difference between the results obtained with a bone that has been boiled for one minute and those obtained with one that has been boiled for ten minutes. The latter results in less satisfactory, often defective, union.

We have secured solid union with boiled bone after a 4 inch (10.16 cm.) fibular resection and with the powdered calcium in other bones after preliminary alkalinization with hundredth-normal solution of sodium carbonate.

In delayed union percussion and damming depend on biochemical changes secondary to vascular changes. In the fracture of the femoral neck in which union occurs only if strain is borne in such wide abduction that there is a jamming together of the fragments of the neck instead of a shearing strain on the fibrous union, as in ordinary weight bearing, the explanation lies in the torsional strain present in the latter instance, which decreases the circulatory efficiency of the soft tissues.

In all these situations the circulatory factor is the difficult one to analyze. For example, Morton has published two analyses of the effect of venous interference on the healing of fractures with diametrically different solutions.

I believe that the effect of diathermy is purely theoretical and lacks adequate clinical or experimental support.

DR. EDWARD L. COMPERE, Chicago: Dr. Murray's interesting explanation of the biochemical factors in the healing of fractures can be accepted if one also recognizes the influence of the osteoblasts themselves acting in the medium which he has described.

Dr. William Stewart, working as a Fellow in orthopedic surgery at the University of Chicago, carried out a series of experiments similar to those made by Dr. J. Albert Key of St. Louis, with the exception that he not only removed a segment of bone from the ulna and the tibia but removed the periosteum as well. The experiments were well controlled. On the one side he placed the calcium salts which had been recommended by Dr. Murray, and on the other side he replaced the fragments of bone or an entire section of bone as in the cases described by Dr. Key. In one series of experiments the calcium salts were put into bags made from fascia lata before being placed in the bone defect. In each instance all the calcium salts were absorbed, and union did not occur in a single instance. When bone that had been boiled long enough (from fifteen to twenty minutes) to destroy the bone cells was used instead of the calcium salts, it also failed to bring about union. It is known that if the periosteum is stripped and a section of bone excised, as shown by Dr. Key in his controls, the defect may be repaired, but in the experiments under consideration the periosteum as well as the bone was removed. All the chemical factors enumerated by Dr. Murray should have been present and the calcium salts were available, but no bone was formed and the calcium was absorbed.

The belief held in the clinics of the University of Chicago is that one important factor in the healing of fractures in nonunion, and particularly in such cases as congenital nonunion, is the presence of living bone cells. The use of the massive bone graft is preferred in such cases, partly because of the splinting effect of the graft.

I agree with Dr. Key that in cases in which the serum calcium and inorganic phosphates and the p_H of the blood are normal living bone cells acting in the ideal medium described by Dr. Murray should be capable of taking the calcium salts from the blood stream and bringing about union, without the addition of any inorganic salts.

I believe that there is an important element to be found in living bone which is not present either in boiled bone or in the inorganic calcium salts.

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QUANTITATIVE STUDY OF THE RATE OF HEALING IN BONE

II. NORMAL RATE OF HEALING

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It is essential that the normal rate of healing be definitely established before any attempt is made to determine the effect of varous conditions and substances on the rate of healing. Once this normal rate is established it should be comparatively easy to estimate the amount of variation produced by such factors as diet, incomplete mobilization of fractured bones, the injection or deposit of substances at the site of fracture and all the other procedures which have been advocated to increase the rate of healing in bone and prevent nonunion.

Although the results reported in this article appear to establish the normal time required for healing, it is proposed to recheck them with the results obtained in experiments on another series of animals, in which more factors are held constant, before this rate of healing is accepted as a standard with which to compare variations from the normal.

The method used in this study has been described in a previous publication.[1] Three factors of strength were measured in each bone, i. e., tensile strength, resistance to torsion and resistance to bending. The data for each of these measures, as well as the data for weight of the bone, were analyzed. This analysis of data was made under the direction of Dr. Edith Boyd of the Institute of Child Welfare and the department of anatomy.

TENSILE STRENGTH

The data were separated into two categories: (1) those concerning nonfractured ulnas and (2) those concerning fractured ulnas. The latter group of bones was subdivided into: (*a*) those which healed within from nine to twenty days, (*b*) those which healed within from twenty to forty days and (*c*) those which healed within from forty to

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1. Peyton, W. T.; Anderson, U. S., and Laymon, C. W.: Quantitative Study of the Rate of Healing in Bone: I. Description of Method, Arch. Surg. **29**:23 (July) 1934.

TABLE 1.—*Tensile Strength and Weight of Bone in Nonfractured and Fractured Ulna*

Rabbit	Right Nonfractured Ulna		Days Required for Healing	Left Fractured Ulna	
	Weight of Bone, Gm.	Tensile Strength, Kg.		Weight of Bone, Gm.	Tensile Strength, Kg.
101	1.620	45.4	8	1.880	....
96	1.450	45.4	9	1.650	5.0*
99	1.600	31.8	11	1.850	2.7
13	1.810	23.6	12	2.090	2.7
8	1.750	28.7	12	2.300	3.4
100	1.800	43.5	12	2.200	5.0
83	1.750	52.4	13	1.850	3.2*
11	1.790	25.9	14	1.950	4.1
17	1.550	39.7	14	2.200	3.4
85	1.050	29.0	15	1.350	4.1*
84	1.200	42.6	16	1.500	7.3*
78	1.600	44.9	17	1.900	5.4*
74	.....	47.2	17	.....	7.3*
88	2.500	51.3	17	2.280	3.2*
28	2.300	23.4	17	2.900	15.4
5	2.100	26.8	17	1.910	4.5
21	2.150	41.3	18	2.550	13.6
22	1.550	29.5	18	1.450	11.3
6	1.210	21.9	18	1.360	....
18	1.150	....	19	1.600	6.8
19	1.500	22.7	20	2.000	22.7
60	1.100	28.1	20	1.600	10.9*
7	1.670	23.1	20	1.960	9.9*
15	1.900	25.4	21	2.350	8.2
55	.....	45.4	21	.....	....
10	1.570	16.9	22	1.750	0.0
48	1.300	40.8	23	.....	....
93	1.540	44.7	23	1.780	17.9*
91	1.630	44.3	23	1.800	26.3*
92	.....	42.2	24	.....	11.8*
94	.....	46.5	25	.....	13.6*
95	.....	23.8	26	.....	13.6*
96	.....	38.1	27	.....	32.7*
2	1.675	29.3	28	1.960	14.3
30	1.950	53.3	29	2.000	9.1*
82	.....	29.5	29	.....	15.4*
31	1.600	39.9	29	.....	....
81	.....	29.5	30	.....	11.8
87	.....	29.9	31	.....	16.3*
1	1.350	14.9	33	1.440	....
77	1.550	51.5	34	1.960	....
76	1.600	33.6	34	1.850	26.3*
73	.....	36.3	36	.....	25.6*
72	.....	32.5	37	.....	29.9
71	.....	31.3	38	.....	30.8*
23	1.500	....	39	1.425	26.8*
20	1.050	24.0	40	1.300	7.3
90	.....	25.6	42	.....	27.9*
102	.....	47.2	43	.....	19.5
89	.....	31.8	45	.....	28.4*
24	.....	36.3	46	.....	13.4*
80	.....	20.0	47	.....	....
79	.....	20.9	49	.....	20.0*
70	.....	47.2	50	.....	20.9*
69	.....	42.6	52	.....	30.2*
68	.....	46.4	56	.....	24.9
65	.....	20.9	58	.....	24.9*
63	.....	38.8	61	.....	20.9
62	.....	32.0	63	.....	25.6
67	.....	40.4	66	.....	26.3
53	.....	34.2	66	.....	19.5*
106	1.538	27.7	77	1.760	5.7*
107	1.791	45.4	93	2.085	40.8*
105	1.770	40.8	96	.....	17.7
113	1.228	20.9	94	1.265	18.0*
111	1.383	49.3	94	1.962	20.3
112	1.824	24.6	96	2.147	35.6
120	1.333	28.2	100	1.555	30.5*
108	2.070	13.8	107	2.722	20.4*
123	1.880	46.5	108	1.892	32.3*
125	1.802	58.4	108	2.390	20.9
124	1.781	44.5	113	2.116	28.7*
119	2.053	36.6	113	2.040	48.5*

TABLE 1.—*Tensile Strength and Weight of Bone in Nonfractured and Fractured Ulna—Continued*

Rabbit	Right Nonfractured Ulna		Days Required for Healing	Left Fractured Ulna	
	Weight of Bone, Gm.	Tensile Strength, Kg.		Weight of Bone, Gm.	Tensile Strength, Kg.
122	1.590	45.9	114	1.726	24.2*
121	1.524	39.6	114	1.586	19.5*
110	.....	28.4	118	.....	24.5
109	2.145	29.7	125	2.300	23.1*
117	1.795	36.1	125	2.115	36.1
118	1.401	52.7	131	1.565	41.4
114	2.105	36.6	135	2.334	29.4
115	1.900	55.7	138	1.927	20.9*
116	1.625	55.0	138	1.800	20.9*
134	1.885	70.2	139	2.385	36.3*
135	1.971	84.6	140	2.141	44.8
137	1.576	62.9	140	1.857	40.3
133	2.117	62.0	145	2.196	43.8*
132	1.763	38.0	145	2.038	27.9*
131	1.613	64.4	152	1.723	50.0*
126	1.943	56.6	188	3.749	35.2
130	1.906	60.0	188	2.230	47.5
136	1.538	60.6	189	1.605	41.7
120	1.509	43.0	189	1.861	24.9
128	1.957	66.8	191	2.360	50.6*
127	2.202	73.7	191	2.530	25.6*

* Separated at line of the fracture.

two hundred days. The last two groups were combined into those which healed within from twenty to two hundred days.

Measurements of tensile strength were made on the nonfractured right ulnas of ninety-two animals and on the fractured left ulnas of eighty-five animals. The subdivisions of the group of fractured ulnas were made according to the number of days intervening between the time of the fracture and the killing of the animal, when the measurements were made.

The data are listed in table 1; they are arranged according to the number of days the animal lived after the fracture was produced.

A regression line formula was computed for the group of nonfractured ulnas and for each of the subdivisions of the group of fractured ulnas. The regression line and the individual observations for the group of nonfractured ulnas are shown in figure 1 *A*. The regression line indicates an increase in the tensile strength of the nonfractured ulna during the period of study. Since the average span of life in the rabbit is from five to six years, two hundred days represents a considerable part of the life of this animal. Therefore, the increase noted in tensile strength is probably due to changes caused by age. These changes may have been due to increased weight or to physical or chemical changes in the bone. That they were not due to increase in weight but rather to physical or chemical changes was indicated by a partial correlation of the data for the nonfractured ulna. This partial correlation was determined for tensile strength, weight and time the animal lived after the operation. It is especially indicated by the standard error of tensile strength when this is computed with variable weight and

time, with the constant weight and variable time, with the constant time and the variable weight and with constant weight and time. The results are given in the section "Comment."

The regression line for the nonfractured group is compared with the data for the fractured group in figure 1 *B*, which includes a field graph of the data for the nonfractured ulnas and a point-to-point curve through the mean values for the tensile strength of the fractured ulnas, computed for ten and twenty day intervals. These groups of data for the fractured ulnas, the number of observations made and the means are as follows:

Days required for healing	10-20	20-30	30-40	40-60	60-80	80-100	100-120	120-140	140-160	160-180	180-200
Number of observations	18	13	7	10	5	5	10	9	5	0	6
Mean.....	6.0	15.9	24.7	21.7	19.6	26.5	27.1	29.7	41.4	0	37.6

The point-to-point curve shows a rapid increase in the tensile strength of the healing bone until after the thirtieth day of healing;

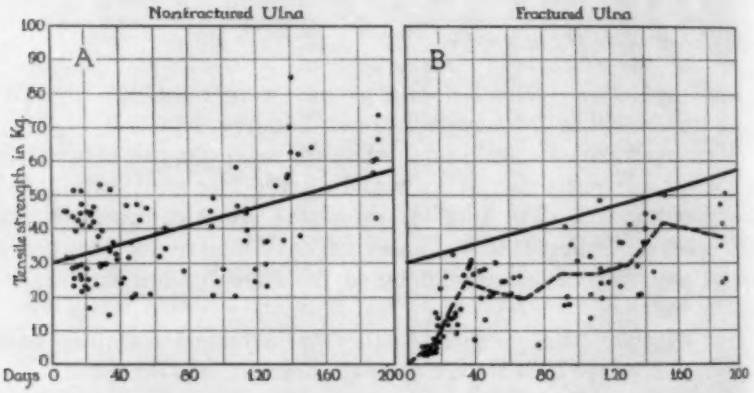

Fig. 1.—*A*, graph for the tensile strength of the nonfractured ulna, with regression line (formula: TS [tensile strength] = 30.2736 + 0.137 D [days]). *B*, graph for tensile strength of the fractured ulna. The broken line is a point-to-point curve through mean values computed for ten and twenty day intervals; the unbroken line is the regression line of the nonfractured ulna.

thereafter the increase in tensile strength is approximately that found in the nonfractured ulna and is therefore probably due to the same changes in the bone.

In order to check this observation, regression line formulas were computed for certain subdivisions of the fractured group, i. e., bones which required from nine to twenty days for healing (eighteen cases), those which required from twenty to forty days (twenty cases), those requiring from forty to two hundred days (forty-seven cases) and those requiring from twenty to two hundred days (sixty-seven cases). These regression lines are shown in figure 2. The regression line of the control group is included for comparison. This demonstrates a rapid increase in

tensile strength between the ninth and twentieth day after fracture and a similar increase between the twentieth and fortieth day of healing, but after the fortieth day of healing there appeared to be no tendency for the bone to regain its original strength. It remained definitely weaker, gaining strength at approximately the same rate shown by the nonfractured bone in which there were changes due to age. Therefore, it may be stated that, so far as tensile strength is concerned, healing in the ulna of the rabbit does not reproduce the original strength of the bone, but it is terminated within less than forty days.

In taking these measurements on eighty-five previously fractured ulnas, not all were found to be separated through the healing fracture; instead, the bone in part of them was separated or pulled apart at some other point. In the earlier experiments, no record was kept of the point of separation. Later, however, a record was kept. Forty-nine

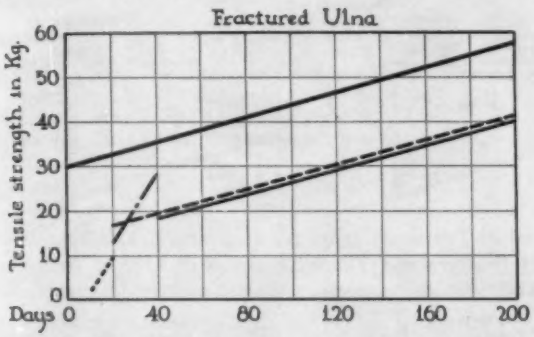

Fig. 2.—Regression lines for tensile strength of the fractured ulna. The line with short dashes indicates the period of from nine to twenty days (formula: TS = 5.26 + 0.7573 D); the line with the long and short dashes, the period of from twenty to forty days (formula: TS = —3.13 + 0.7849 D); the lower unbroken line, the period of from forty to two hundred days (formula: TS = 14.06 + 0.1335 D), and the line with long dashes, the period of from twenty to two hundred days (formula: TS = 14.68 + 0.1299 D); the upper unbroken line is the regression line of the nonfractured ulna.

bones were recorded as having separated at the line of fracture (indicated by the asterisk in table 1), and in thirty-six cases either no notation concerning the point of separation was made or the bones were recorded as having separated outside the line of fracture. These thirty-six cases make up the group called fractured ulnas not separated at the line of fracture.

For the purpose of analysis, the data for both groups—ulnas not separated at the line of fracture and those separated at this line—were subdivided according to the number of days the animal lived after the operation before it was killed. These data are as follows:

	Not Separated at Line of Fracture				Separated at Line of Fracture			
Days required for healing.....	9-20	20-40	40-200	20-200	9-20	20-40	40-200	20-200
Number of cases in group.....	11	5	20	25	7	15	27	42

TABLE 2.—*Means of Tensile Strength for Nonfractured and Fractured Ulnas*

Nonfractured Ulna		Fractured Ulna					
Number of Cases	Mean ± Standard Error, Degrees	Number of Cases	Duration of Healing, Days	Mean ± Standard Error, Degrees	Difference ± Standard Error	R	P
92	39.32 ± 1.4523	18	9-20	6.02 ± 0.8627	33.30 ± 1.6892	19.71	>0.00
		20	20-40	18.85 ± 1.7911	20.47 ± 2.3059	8.88	>0.00
		47	40-200	28.46 ± 1.5593	10.86 ± 2.1309	5.10	>0.00
		67	20-200	25.59 ± 1.3316	13.73 ± 1.9704	6.97	>0.00

TABLE 3.—*Regression Coefficients of Tensile Strength and Time for Nonfractured and Fractured Ulnas*

Nonfractured Ulna		Fractured Ulna					
Number of Cases	b ± Standard Error	Number of Cases	Duration of Healing, Days	b ± Standard Error	Difference ± Standard Error	R	P
92	0.1370 ± 0.0230	18	9-20	0.7573 ± 0.2692	−0.6203 ± 0.2702	2.30	0.02
		20	20-40	0.7849 ± 0.2500	−0.6479 ± 0.2511	2.58	0.01
		47	40-200	0.1335 ± 0.0288	0.0035 ± 0.0369	0.09	0.93
		67	20-200	0.1290 ± 0.0190	0.0071 ± 0.0304	0.23	0.82

TABLE 4.—*Means of Tensile Strength for Fractured Ulnas Separated Outside Line of Fracture and Those Separated at Line of Fracture*

Fractured Ulna Not Separated at Line of Fracture			Fractured Ulna Separated at Line of Fracture				
Number of Cases	Duration of Healing, Days	Mean ± Standard Error, Degrees	Number of Cases	Duration of Healing, Days	Mean ± Standard Error, Degrees	Difference ± Standard Error	R	P
11	9-20	6.63 ± 1.3236	7	9-20	5.07 ± 0.6085	1.56 ± 1.4568	1.07	0.28
5	20-40	17.28 ± 3.5195	15	20-40	19.33 ± 2.0707	−1.95 ± 4.0835	0.48	0.63
20	40-200	29.24 ± 2.3099	27	40-200	27.89 ± 2.0958	1.35 ± 3.1190	0.43	0.67
25	20-200	26.87 ± 2.1920	42	20-200	24.83 ± 1.6634	2.04 ± 2.7517	0.74	0.46

TABLE 5.—*Regression Coefficients of Tensile Strength and Time of Healing for Fractured Ulnas Separated Outside Line of Fracture and Those Separated at Line of Fracture*

Fractured Ulna Not Separated at Line of Fracture			Fractured Ulna Separated at Line of Fracture				
Number of Cases	Duration of Healing, Days	b ± Standard Error	Number of Cases	Duration of Healing, Days	b ± Standard Error	Difference ± Standard Error	R	P
11	9-20	1.1077 ± 0.3673	7	9-20	0.1503 ± 0.2550	0.9574 ± 0.4471	2.14	0.03
5	20-40	0.6329 ± 0.6296	15	20-40	0.8401 ± 0.2899	−0.2072 ± 0.6933	0.30	0.76
20	40-200	0.1494 ± 0.0357	27	40-200	0.1176 ± 0.0454	0.0318 ± 0.0574	0.55	0.59
25	20-200	0.1461 ± 0.0277	42	20-200	0.1191 ± 0.0285	0.0270 ± 0.0400	0.68	0.51

Regression line formulas were computed for each of these groups. The regression lines which they represent and a field graph of the distribution of the cases for both the ulnas which separated outside the line of fracture and those which separated through the site of fracture are shown in figure 3.

Comparison of the means and regression coefficients for all the regression lines computed for the data on tensile strength is made in tables 2, 3, 4 and 5.

TORSION

The data obtained in measuring resistance to torsion are given in table 6. The analysis of these data was more difficult than the analysis of the data for tensile strength, because the weight added was not the same in each experiment. This difficulty was surmounted in the following way: It was obvious that a straight line could be fitted to the

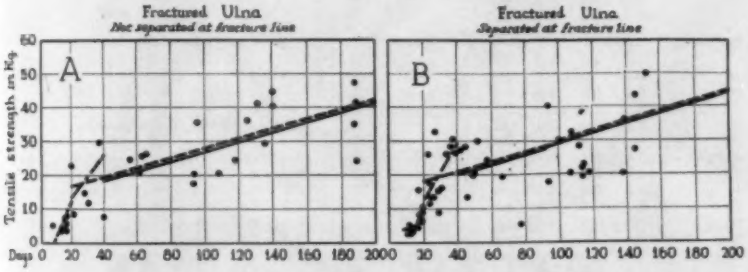

Fig. 3.—*A*, graph for tensile strength of the fractured ulna not separated at the line of fracture. The line with short dashes indicates the period of from nine to twenty days (formula: TS = 9.89 + 1.1077 D); the line with long and short dashes, the period of from twenty to forty days (formula: TS = 0.17 + 0.6329 D); the unbroken line, the period of from forty to two hundred days (formula: TS = 12.34 + 0.1494 D), and the line with long dashes, the period of from twenty to two hundred days (formula: TS = 12.85 + 0.1461 D). *B*, graph for tensile strength of the fractured ulna separated at the line of fracture. The line with short dashes indicates the period of from nine to twenty days (formula: TS = 2.84 + 0.1503 D); the line with long and short dashes, the period of from twenty to forty days (formula: TS = 4.42 + 0.8401 D); the unbroken line, the period of from forty to two hundred days (formula: TS = 15.67 + 0.1176 D), and the line with long dashes, the period of from twenty to two hundred days (formula: TS = 15.67 + 0.1191 D).

data if the measurements taken after addition of the first 10 Gm. of weight were not included. It seemed justifiable to assume that the readings taken after the addition of 10 Gm. of weight were too low because of resistance other than elasticity of the bone in the experimental set-up. They were therefore disregarded in calculatng the regression line for these data. A scatter diagram of the measurements

TABLE 6.—*Resistance to Torsion of Nonfractured and Fractured Ulnas*

	Nonfractured Ulna								Fractured Ulna							
	Weight Added, Gm.								Weight Added, Gm.							
Rabbit	0 to 10	0 to 20	20 to 40	40 to 60	60 to 80	80 to 100	40 to 90	Days Required for Healing	0 to 10	0 to 20	20 to 30	30 to 40	40 to 60	60 to 80	80 to 100	40 to 90
	Torsion, Degrees								Torsion, Degrees							
101	—	0.4	0.3	0.5	—	—	—	8	—	—	—	Too weak		—	—	—
98	—	0.4	0.5	0.5	0.5	0.6	—	9	6.2	7.0	6.0	—	—	—	—	—
99	—	0.3	0.4	0.4	0.5	0.5	—	11	39.2	—	—	Too weak		—	—	—
8	—	—	0.9	1.0	0.8	0.7	—	12	—	—	—	Too weak		—	—	—
13	—	—	0.9	1.0	1.0	1.1	—	12	—	—	—	Too weak		—	—	—
100	—	0.2	0.3	0.4	0.3	0.4	—	12	3.1	6.1	—	—	—	—	—	—
83	—	0.3	0.3	0.3	0.4	0.4	—	13	10.5	12.0	4.0	—	—	—	—	—
11	—	—	0.5	0.9	1.0	0.8	—	14	—	—	—	1.3	1.7	2.0	—	—
17	—	—	1.5	2.5	1.0	2.0	—	14	2.9	5.5	—	Too weak		—	—	—
85	—	0.6	0.8	0.9	0.8	1.1	—	15	2.2	5.7	—	—	—	—	—	—
84	—	0.5	0.7	0.8	0.7	0.7	—	16	1.5	3.2	2.0	—	—	—	—	—
28	—	0.5	0.5	0.4	0.4	0.5	—	17	—	0.4	—	0.7	0.6	0.7	0.9	—
74	—	0.6	0.6	0.6	0.6	0.7	—	17	2.5	6.5	5.0	—	—	—	—	—
88	—	0.3	0.4	0.5	—	—	—	17	0.9	2.2	—	—	—	—	—	—
5	—	—	0.5	0.4	0.4	0.7	—	17	—	0.8	—	0.4	0.6	0.9	—	—
78	—	0.3	0.5	0.4	0.5	0.5	—	17	3.0	6.0	5.0	—	—	—	—	—
22	—	0.8	1.4	2.2	2.7	2.6	—	18	—	0.5	—	0.9	1.1	1.1	—	—
21	—	0.5	0.5	0.6	0.5	0.7	—	18	—	0.7	—	0.8	0.8	1.0	—	—
6	—	—	0.7	0.6	0.9	0.9	—	18	—	—	—	—	—	—	—	—
18	—	—	—	—	—	—	—	19	3.4	6.0	2.4	—	—	—	—	—
7	—	—	0.9	1.0	0.9	1.0	—	20	—	—	—	1.6	1.9	1.6	—	—
19	—	0.9	1.0	1.2	1.0	1.9	—	20	—	0.6	—	1.0	1.0	0.7	0.9	—
60	—	0.8	0.9	0.8	1.2	1.3	—	20	—	1.2	—	2.1	1.9	2.3	—	—
15	—	0.3	0.4	0.5	0.5	0.4	—	21	—	0.9	—	1.2	1.1	1.2	1.1	—
55	—	0.4	0.5	0.6	0.5	0.6	—	21	Displacement of fragments						—	—
10	—	—	0.5	0.7	0.6	0.9	—	22	—	—	—	0.9	0.7	0.6	0.9	—
48	—	0.4	0.4	0.4	0.5	0.5	—	23	Osteomyelitis				—	—	—	—
93	—	0.4	0.3	0.6	—	—	—	23	0.4	0.8	0.5	—	—	—	—	—
91	—	0.3	0.4	0.4	—	—	—	23	0.3	0.8	0.2	—	—	—	—	—
92	—	0.4	0.3	0.4	—	—	—	24	0.3	0.6	0.5	—	—	—	—	—
94	—	0.3	0.5	0.5	—	—	—	25	0.2	0.5	0.4	—	—	—	—	—
95	0.2	0.6	—	—	—	—	—	26	0.4	0.9	—	—	—	—	—	—
96	0.3	0.5	—	—	—	—	—	27	0.3	—	—	—	—	—	—	—
2	—	1.1	1.3	1.2	1.3	1.4	—	28	—	0.5	—	0.7	0.8	0.53	—	—
82	0.2	0.4	—	—	—	—	—	29	0.3	0.5	—	—	—	—	—	—
31	—	0.4	0.3	0.5	0.6	0.5	—	29	Slough of soft parts over fracture							
30	—	0.3	0.5	0.4	0.5	0.5	—	29	0.8	1.7	0.5	1.1	—	—	—	—
81	0.3	0.7	—	—	—	—	—	30	2.1	—	—	—	—	—	—	—
87	0.3	0.5	—	—	—	—	—	31	0.9	—	—	—	—	—	—	—
1	—	—	0.9	1.0	1.1	1.0	—	33	4.1	7.2	3.0	—	—	—	—	—
77	—	0.4	0.3	0.5	—	—	—	34	0.2	0.5	0.3	—	—	—	—	—
76	—	0.3	0.4	0.5	—	—	—	34	0.2	0.4	0.3	—	—	—	—	—
73	—	0.5	0.5	0.5	—	—	—	36	0.3	0.6	0.3	—	—	—	—	—
72	0.2	0.4	—	—	—	—	—	37	0.3	0.6	—	—	—	—	—	—
71	0.2	0.4	—	—	—	—	—	38	0.2	0.5	—	—	—	—	—	—
23	—	1.0	1.1	1.1	1.5	1.4	—	39	—	1.0	—	1.2	1.3	1.3	1.3	—
20	—	2.0	1.0	2.6	1.9	—	—	40	—	1.0	—	1.3	1.2	1.4	—	—
90	0.2	0.4	—	—	—	—	—	42	0.1	0.3	—	—	—	—	—	—
102	0.2	0.4	—	—	—	—	—	43	0.2	0.4	—	—	—	—	—	—
89	0.2	0.6	—	—	—	—	—	45	0.3	0.5	—	—	—	—	—	—
24	0.2	0.4	—	—	—	—	—	46	0.2	—	—	—	—	—	—	—
80	0.4	0.8	—	—	—	—	—	47	0.5	1.1	—	—	—	—	—	—
79	0.3	0.6	—	—	—	—	—	49	0.3	0.6	—	—	—	—	—	—
70	0.1	0.3	—	—	—	—	—	50	0.2	0.4	—	—	—	—	—	—
69	0.2	0.4	—	—	—	—	—	52	0.1	0.2	—	—	—	—	—	—
68	0.4	0.7	—	—	—	—	—	56	0.2	0.5	—	—	—	—	—	—
65	0.2	0.4	—	—	—	—	—	58	0.2	0.5	—	—	—	—	—	—
63	0.3	0.7	—	—	—	—	—	61	0.2	0.5	—	—	—	—	—	—
62	0.3	0.6	—	—	—	—	—	63	0.3	0.6	—	—	—	—	—	—
53	0.2	0.4	—	—	—	—	—	66	0.3	0.5	—	—	—	—	—	—
67	0.3	0.7	—	—	—	—	—	66	0.3	0.5	—	—	—	—	—	—
106	—	—	—	0.2	—	—	—	77	—	—	—	—	0.3	—	—	—
105	—	—	—	0.6	—	—	—	93	—	—	—	—	0.5	—	—	—
107	—	—	—	0.8	—	—	—	93	—	—	—	—	0.4	—	—	—
111	—	—	—	0.7	—	—	—	94	—	—	—	—	0.3	—	—	—
113	—	—	—	0.8	—	—	—	94	—	—	—	—	0.8	—	—	—
112	—	—	—	0.4	—	—	—	96	—	—	—	—	0.9	—	—	—
120	—	—	—	—	—	—	1.3	100	—	—	—	—	—	—	—	1.0
108	—	—	—	0.5	—	—	—	107	—	—	—	—	0.3	—	—	—
123	—	—	—	—	—	—	0.7	108	—	—	—	—	—	—	—	0.5
125	—	—	—	—	—	—	0.9	108	—	—	—	—	—	—	—	0.4

TABLE 6.—*Resistance to Torsion of Nonfractured and Fractured Ulnas—Continued*

Rabbit	Nonfractured Ulna: Weight Added, Gm. 0 to 10	0 to 20	20 to 40	40 to 60	60 to 80	80 to 100	40 to 90	Days Required for Healing	Fractured Ulna: Weight Added, Gm. 0 to 10	0 to 20	20 to 30	30 to 40	40 to 60	60 to 80	80 to 100	40 to 90
	Torsion, Degrees								Torsion, Degrees							
124	—	—	—	—	—	—	0.8	113	—	—	—	—	—	—	—	0.3
119	—	—	—	—	—	—	0.5	113	—	—	—	—	—	—	—	0.7
122	—	—	—	—	—	—	1.0	114	—	—	—	—	—	—	—	1.0
121	—	—	—	—	—	—	0.8	114	—	—	—	—	—	—	—	1.2
110	—	—	—	0.5	—	—	—	118	—	—	—	—	0.3	—	—	—
109	—	—	—	0.4	—	—	—	125	—	—	—	—	0.5	—	—	—
117	—	—	—	0.5	—	—	—	125	—	—	—	—	0.6	—	—	—
116	—	—	—	—	—	—	0.9	131	—	—	—	—	—	—	—	0.7
114	—	—	—	—	—	—	0.5	135	—	—	—	—	—	—	—	0.5
115	—	—	—	—	—	—	0.4	138	—	—	—	—	—	—	—	0.5
116	—	—	—	—	—	—	1.8	138	—	—	—	—	—	—	—	0.8
134	—	—	—	—	—	—	0.7	139	—	—	—	—	—	—	—	0.4
137	—	—	—	—	—	—	0.7	140	—	—	—	—	—	—	—	0.3
135	—	—	—	—	—	—	0.6	140	—	—	—	—	—	—	—	0.4
133	—	—	—	—	—	—	0.8	145	—	—	—	—	—	—	—	1.9
132	—	—	—	—	—	—	0.4	145	—	—	—	—	—	—	—	0.4
131	—	—	—	—	—	—	0.8	152	—	—	—	—	—	—	—	0.5
126	—	—	—	—	—	—	1.1	188	—	—	—	—	—	—	—	2.5
130	—	—	—	—	—	—	0.7	188	—	—	—	—	—	—	—	0.5
136	—	—	—	—	—	—	0.9	189	—	—	—	—	—	—	—	0.9
129	—	—	—	—	—	—	2.2	189	—	—	—	—	—	—	—	0.7
128	—	—	—	—	—	—	1.2	191	—	—	—	—	—	—	—	0.5
127	—	—	—	—	—	—	0.9	191	—	—	—	—	—	—	—	0.5

for the group of nonfractured ulnas and the regression line are included in figure 4.

This regression line was then considered as the base line, and the degrees of torsion of the nonfractured ulna were plotted against the days the rabbit lived after the operation (fig. 5 *A*). It was again considered as the base line in figure 5 *B*, in which the degrees of torsion of the fractured ulna were plotted against the days the rabbit lived after the operation. A curve was drawn and smoothed through the means as computed for ten day intervals. This would indicate that the fractured bone regained normal resistance to torsion approximately sixty days after fracture.

BENDING

The data obtained in measuring resistance to bending are given in table 7. The analysis of these data was made in a manner similar to that of the analysis of the data for torsion. Here also the weights added were not the same in each experiment. It was obvious that a straight line could be fitted well to the data for the nonfractured ulna. This was done by calculating the regression line for these data. The regression line and a scattered diagram of the data are shown in figure 6.

As in the analysis of the data for torsion, this regression line was considered as the base line, and the degrees of bending of the nonfractured ulna were plotted around it against the days the rabbit lived

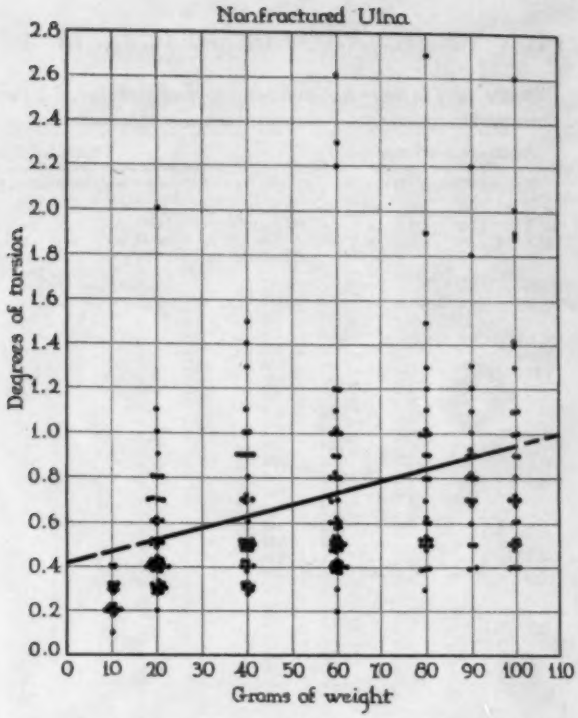

Fig. 4.—Graph for resistance to torsion in the nonfractured ulna. The regression line was computed after excluding the data obtained on addition of the first 10 Gm. of weight (formula: DT [degrees of torsion] = 0.4316 + 0.0053 W [weight]).

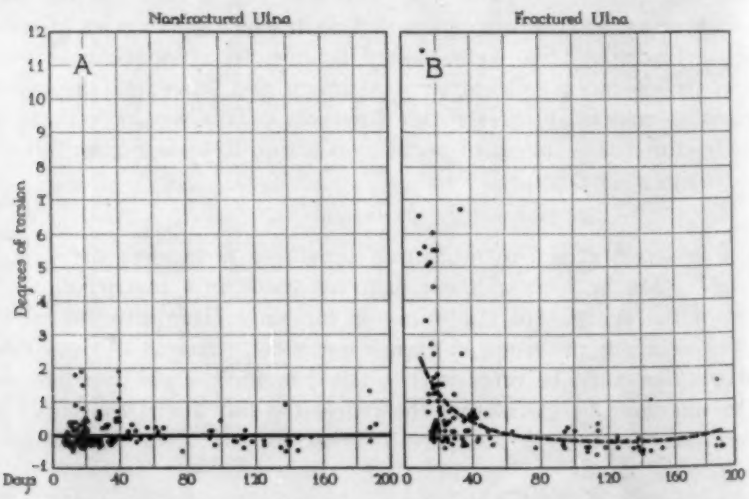

Fig. 5.—*A*, graph for resistance to torsion in the nonfractured ulna, plotted around the regression line of figure 4 as the base line (formula: DT = 0.4136 + 0.0053 W). *B*, graph for resistance to torsion in the fractured ulna, plotted around the regression line of figure 4 as the base line. The smoother point-to-point curve is through the means computed for ten day intervals.

TABLE 7.—*Resistance to Bending of Nonfractured and Fractured Ulnas*

Rabbit	Right Nonfractured Ulna — Weight Added, Gm.						Days Required for Healing	Left Fractured Ulna — Weight Added, Gm.					
	0 to 500	480.5 to 980.5	500 to 1,000	1,000 to 1,500	1,500 to 2,000	2,000 to 2,500	2,500 to 3,000		0 to 500	480.5 to 980.5	500 to 1,000	1,000 to 1,500	1,500 to 2,000	2,000 to 2,500	2,500 to 3,000
	Torsion, Degrees								Torsion, Degrees						
101	—	—	0.5	0.8	1.4	3.0	2.5	8	—	—	Too weak	—	—	—	—
98	—	—	6.0	4.0	4.0	3.0	2.5	9	—	—	—	2.5	22.5	63.0	65.0
99	—	—	1.2	4.3	2.7	2.0	2.0	11	—	—	—	25.0	43.0	36.0	—
100	—	—	3.5	3.3	2.2	2.6	3.2	12	—	—	—	16.0	21.0	35.0	—
83	—	—	0.5	0.5	1.1	1.1	1.8	13	—	—	—	3.0	13.0	85.0	—
17	—	—	10.1	6.7	—	—	—	14	—	—	Too weak	—	—	—	—
85	—	—	2.0	1.5	2.5	1.7	2.3	15	—	—	—	12.5	17.0	15.0	—
84	—	—	1.5	1.4	0.8	1.7	2.1	16	—	—	—	9.0	17.5	31.5	—
28	—	—	1.0	1.0	1.0	1.0	—	17	—	—	3.0	2.0	7.0	—	—
74	—	—	1.5	0.7	2.0	2.7	5.8	17	—	—	—	19.0	34.0	55.0	—
88	—	—	1.0	1.0	1.2	—	—	17	—	—	—	9.0	30.5	83.0	—
5	—	—	1.2	—	—	—	—	17	—	—	—	—	—	—	—
78	—	—	—	2.0	1.5	1.0	1.5	17	—	—	22.0	20.0	26.0	—	—
22	—	—	4.0	5.0	4.0	—	—	18	—	—	6.0	11.5	—	—	—
19	—	—	2.0	3.0	1.5	—	—	20	—	—	—	—	—	—	—
60	—	—	—	—	—	—	—	20	—	—	8.0	8.5	8.5	9.0	12.0
15	—	—	1.6	1.1	—	—	—	21	—	—	—	—	—	—	—
55	—	—	1.3	3.4	2.6	1.2	3.8	21	—	—	—	—	—	—	—
48	—	—	1.0	1.0	1.0	1.0	1.0	23	—	—	—	—	—	—	—
93	—	—	0.5	0.7	0.8	—	—	23	—	—	2.2	5.2	4.5	—	—
91	—	—	0.8	1.0	1.0	—	—	23	—	—	—	0.6	1.2	1.0	—
92	—	—	1.8	1.2	1.4	—	—	24	—	—	3.6	6.1	6.0	—	—
94	—	—	3.9	2.2	5.1	—	—	25	—	—	1.8	3.2	3.3	—	—
95	—	—	0.4	—	—	—	—	26	—	—	3.2	4.3	—	—	—
96	—	—	1.2	—	—	—	—	27	—	—	3.2	—	—	—	—
2	—	—	—	—	—	—	—	28	12.8	—	5.3	—	—	—	—
82	—	—	2.3	—	—	—	—	29	—	—	2.3	2.4	—	—	—
31	—	—	2.0	0.4	2.8	0.8	3.0	29	—	—	—	—	—	—	—
30	—	—	0.8	1.0	1.0	1.1	0.9	29	—	—	—	5.0	13.0	30.0	46.0
81	—	—	0.5	—	—	—	—	30	—	—	8.8	—	—	—	—
87	—	—	1.3	—	—	—	—	31	—	—	2.1	—	—	—	—
1	—	—	5.8	—	—	—	—	33	—	—	—	—	—	—	—
77	—	—	0.2	1.0	2.0	2.0	—	34	—	—	1.5	1.8	1.7	1.8	—
76	—	—	1.1	3.1	3.3	—	—	34	—	—	—	0.7	0.8	3.0	—
73	—	—	2.2	2.0	1.0	—	—	36	—	—	1.3	1.0	2.0	—	—
72	—	—	1.2	—	—	—	—	37	—	—	2.4	2.6	—	—	—
71	—	—	1.3	—	—	—	—	38	—	—	1.4	1.1	—	—	—
23	—	—	3.0	1.8	1.7	2.0	—	39	—	—	0.5	3.0	4.5	10.0	—
20	—	—	0.5	1.5	3.0	2.0	—	40	—	—	5.0	6.0	8.5	6.5	—
90	—	—	1.0	—	—	—	—	42	—	—	2.4	—	—	—	—
102	—	—	1.5	—	—	—	—	43	—	—	1.4	—	—	—	—
89	—	—	2.0	—	—	—	—	45	—	—	2.0	—	—	—	—
24	—	—	1.2	—	—	—	—	46	—	—	1.0	—	—	—	—
80	—	—	1.2	—	—	—	—	47	—	—	1.7	—	—	—	—
79	—	—	2.0	—	—	—	—	49	—	—	4.9	—	—	—	—
70	—	—	2.7	—	—	—	—	50	—	—	1.5	—	—	—	—
69	—	—	2.1	—	—	—	—	52	—	—	1.6	—	—	—	—
68	—	—	2.0	—	—	—	—	56	—	—	1.2	—	—	—	—
65	—	—	1.9	—	—	—	—	58	—	—	2.3	—	—	—	—
63	—	—	1.7	—	—	—	—	61	—	—	2.0	—	—	—	—
62	—	—	1.3	—	—	—	—	63	—	—	1.8	—	—	—	—
53	—	—	2.0	—	—	—	—	66	—	—	3.4	—	—	—	—
67	—	—	3.0	—	—	—	—	66	—	—	2.0	—	—	—	—
106	—	1.5	—	—	—	—	—	77	—	3.5	—	—	—	—	—
105	—	2.5	—	—	—	—	—	93	—	—	—	—	—	—	—
107	—	2.0	—	—	—	—	—	93	—	3.0	—	—	—	—	—
111	—	1.5	—	—	—	—	—	94	—	1.3	—	—	—	—	—
113	—	2.5	—	—	—	—	—	94	—	7.0	—	—	—	—	—
112	—	2.8	—	—	—	—	—	96	—	4.6	—	—	—	—	—
120	—	4.0	—	—	—	—	—	100	—	1.5	—	—	—	—	—
108	—	3.5	—	—	—	—	—	107	—	3.5	—	—	—	—	—
123	—	0.7	—	—	—	—	—	108	—	1.5	—	—	—	—	—
125	—	0.5	—	—	—	—	—	108	—	2.0	—	—	—	—	—
124	—	0.5	—	—	—	—	—	113	—	3.5	—	—	—	—	—
119	—	0.5	—	—	—	—	—	113	—	1.0	—	—	—	—	—
122	—	2.5	—	—	—	—	—	114	—	1.0	—	—	—	—	—

TABLE 7.—*Resistance to Bending of Nonfractured and Fractured Ulnas—Continued*

Rabbit	Right Nonfractured Ulna: Weight Added, Gm. 0 to 500	480.5 to 980.5	500 to 1,000	1,000 to 1,500	1,500 to 2,000	2,000 to 2,500	2,500 to 3,000	Days Required for Healing	Left Fractured Ulna: Weight Added, Gm. 0 to 500	480.5 to 980.5	500 to 1,000	1,000 to 1,500	1,500 to 2,000	2,000 to 2,500	2,500 to 3,000
	Torsion, Degrees								Torsion, Degrees						
121	—	1.5	—	—	—	—	—	114	—	3.0	—	—	—	—	—
110	—	2.0	—	—	—	—	—	118	—	2.0	—	—	—	—	—
109	—	4.5	—	—	—	—	—	125	—	4.0	—	—	—	—	—
117	—	1.0	—	—	—	—	—	125	—	2.5	—	—	—	—	—
118	—	1.0	—	—	—	—	—	131	—	1.0	—	—	—	—	—
114	—	2.3	—	—	—	—	—	135	—	4.0	—	—	—	—	—
115	—	1.5	—	—	—	—	—	138	—	1.8	—	—	—	—	—
116	—	1.5	—	—	—	—	—	138	—	6.0	—	—	—	—	—
134	—	1.3	—	—	—	—	—	139	—	1.5	—	—	—	—	—
137	—	1.2	—	—	—	—	—	140	—	6.3	—	—	—	—	—
135	—	2.4	—	—	—	—	—	140	—	2.0	—	—	—	—	—
133	—	0.6	—	—	—	—	—	145	—	4.0	—	—	—	—	—
132	—	2.5	—	—	—	—	—	145	—	2.0	—	—	—	—	—
131	—	1.0	—	—	—	—	—	152	—	2.8	—	—	—	—	—
126	—	0.8	—	—	—	—	—	188	—	5.3	—	—	—	—	—
130	—	2.8	—	—	—	—	—	188	—	3.1	—	—	—	—	—
136	—	3.4	—	—	—	—	—	189	—	3.0	—	—	—	—	—
129	—	2.0	—	—	—	—	—	189	—	4.0	—	—	—	—	—
128	—	2.5	—	—	—	—	—	191	—	2.5	—	—	—	—	—
127	—	1.5	—	—	—	—	—	191	—	1.3	—	—	—	—	—

TABLE 8.—*Means of Weight of Bone for Nonfractured and Fractured Ulnas*

Nonfractured Ulna: Number of Cases	Nonfractured Ulna: Mean ± Standard Error, Degrees	Fractured Ulna: Number of Cases	Fractured Ulna: Duration of Healing, Days	Fractured Ulna: Mean ± Standard Error, Degrees	Difference ± Standard Error	R	P
67	1.6965 ± 0.0399	64	20-200	1.9588 ± 0.0501	−0.2633 ± 0.0640	4.11	>0.00

TABLE 9.—*Regression Coefficients of Weight of Bone and Time of Healing for Nonfractured and Fractured Ulnas*

Nonfractured Ulna: Number of Cases	Nonfractured Ulna: b ± Standard Error	Fractured Ulna: Number of Cases	Fractured Ulna: Duration of Healing, Days	Fractured Ulna: b ± Standard Error	Difference ± Standard Error	R	P
67	0.0015 ± 0.0006	64	20-200	0.0013 ± 0.0008	0.0002 ± 0.0010	0.20	0.84

after the operation (fig. 7 *A*). It was again considered as the base line in figure 7 *B*, in which the degrees of bending of the fractured ulna were plotted against the days the rabbit lived after the operation. A curve was drawn and smoothed through the means as computed for twenty day intervals of healing. This would indicate that the fractured bone had regained normal resistance to bending approximately sixty days after fracture.

WEIGHT OF THE BONE

The data for the weight of the bones are included in table 1 with the data for tensile strength. Figure 8 *B* is a scatter diagram of the data for the weight of the nonfractured ulna plotted against time; the regression line is also shown. It is to be noted that, although there was a great variation in the weight of the bone, there was a progressive increase in weight as the interval between the operation and the killing of the animal was increased. This was probably due to normal growth of the ulna.

Figure 8 *B* is a similar diagram of the data for the fractured ulna and the regression line. It is evident that the fractured ulna was

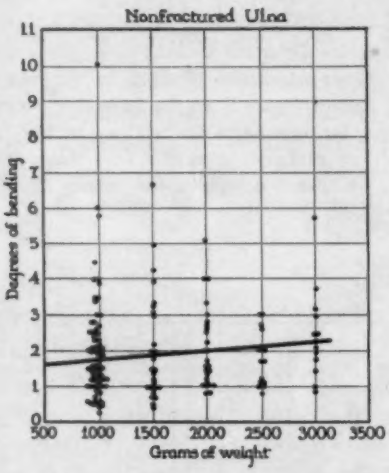

Fig. 6.—Graph for resistance to bending in the nonfractured ulna, with regression line (formula: DB [degree of bending] = 1.7254 + 0.00016 W [weight]).

increased in weight (table 8). There were probably two factors involved in this increase in weight. In the animals killed within the first two or three weeks after the operation this increase was due, either in part or entirely, to callus at the site of the fracture. Later, the callus was, at least in part, absorbed, but synostosis with the ulna was present in most of these healed fractures. In removing the bone this synostosis was cut close to the radius, leaving all the synostoses with the ulna; perhaps at times even a chip of cortex of the radius was left attached to the ulna. In spite of these different factors, the increase in weight with time was so similar to the increase in the unfractured ulna that when their constants are compared no significant difference is demonstrated (table 9).

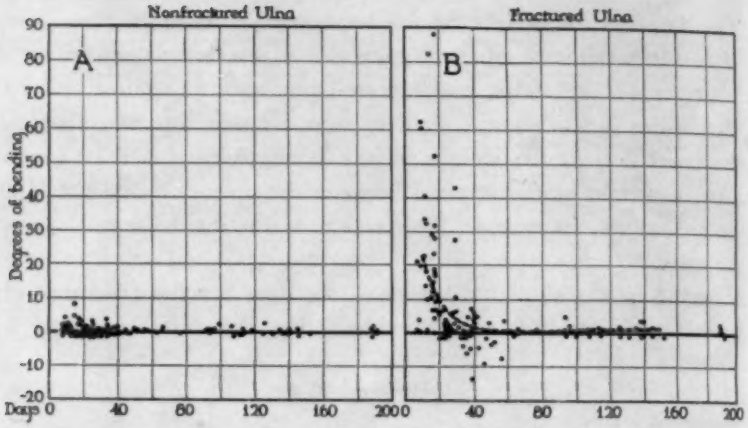

Fig. 7.—*A*, graph for resistance to bending in the nonfractured ulna, plotted around the regression line of figure 6 as the base line (formula: DB = 1.7254 + 0.00016 W). *B*, graph for resistance to bending in the fractured ulna, plotted around the regression line of figure 6 as the base line. The smoothed point-to-point curve is through the means computed for twenty day intervals.

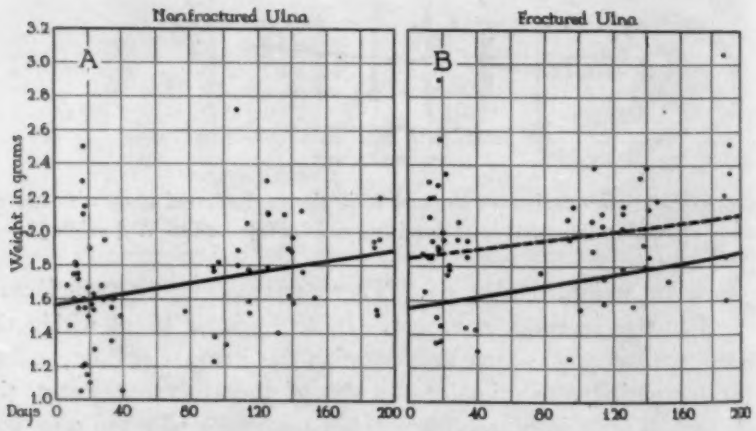

Fig. 8.—*A*, graph for weight of the nonfractured ulna, with the regression line (formula: BW [weight of the bone] = 1.5852 + 0.0015 D). *B*, graph for weight of the fractured ulna, with regression line (broken line) for these data (formula: BW = 1.8616 + 0.0013 D) and the regression line for the nonfractured ulna (unbroken line).

COMMENT

The data analyzed as measures of torsion and bending were obtained by adding weights and taking a reading after the addition of each weight. Readings were also taken as these weights were removed. The data for torsion were analyzed and found to fit well to a straight line, but not as well as the data obtained on the addition of weight. This difference may be due to a third factor, time, which was disregarded in the experiment. Bone obviously has imperfect elasticity and would therefore show a lag in torsion or bending on the addition of weight and perhaps return more slowly after the removal of weight. To correct for this, it would be advisable, in collecting additional data, to take the reading at a constant interval after the addition or removal of weight.

As has been stated, partial correlation between the tensile strength of the nonfractured ulna, weight and time was made to determine what part increase of weight played in the observed increase in tensile strength. The coefficient of correlation was 0.0542, which is not significant; moreover, the standard errors of the array for tensile strength alone and with weight, time and both time and weight held constant were determined. With σ denoting the standard deviation, they are as follows:

Tensile Strength	Standard Error
σ Tensile strength	10.90 ± 0.95
σ Tensile strength	10.90 ± 0.95
σ Tensile strength—time.....	8.46 ± 0.74
σ Tensile strength—time—weight.....	8.44 ± 0.96

From these figures it is evident that the standard error of tensile strength is approximately the same, whether weight is held constant or not, but if time is held constant it is changed by approximately 22 per cent. This indicates that the increased tensile strength in the nonfractured ulna (fig. 1 *A*) is due to physical or chemical changes in the bone that occur with age rather than to increased weight of the bone.

In rechecking these experiments it is proposed to select animals which will have reached approximately the same age at the time they are killed.

SUMMARY AND CONCLUSION

1. It is important to determine the normal rate of healing in bone and its variability before any attempt is made to estimate possible variations.

2. In determining the return of function or strength in healing bone three factors were measured, i. e., tensile strength, resistance to torsion and resistance to bending.

3. The ulna of the nonfractured leg was used as a control.

4. So far as tensile strength is concerned, healing was complete approximately thirty days after fracture in the ulna of the rabbit, but within the limits of this experiment the fractured bone never completely regained the tensile strength present in normal bone of the opposite leg.

5. The fractured ulna of the rabbit was found to have completely regained its resistance to torsion and bending approximately sixty days after fracture.

AMBULATORY TREATMENT OF VARICOSE STATE BY COMBINED LIGATION AND THROMBOSIS BY INJECTION

A STUDY IN END-RESULTS

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The results obtained at the Stanford University Clinics following therapeutic thrombosis of varicose veins by the injection of sclerosing solutions were reported in 1931.[1] Careful examination a year or more following thrombosis disclosed recanalization or recurrence in the thrombosed veins in 98 per cent of all patients examined. In spite of the recurrence of varicosities and recanalization of veins, 54 per cent of the patients had complete relief of all symptoms attributed to the presence of the varicosities and 94 per cent obtained partial or complete relief of symptoms during the period of observation. That the recurrence was due to recanalization of the thrombus, and not to the formation of new veins or enlargement of collateral venous channels, was shown by a microscopic study of veins excised at intervals following thrombosis by injection, and by personal observation and comparison of the recurrent varicose veins with the charted positions of the original varicosities. At that time it was suggested that the venous back pressure in the unthrombosed upper saphenous segment might be the chief contributing factor in the rapid recanalization and recurrence of the thrombosed veins, and that the thrombosis caused by the injection of sclerosing agents might well be supplemented by the proximal ligation of the saphenous vein at the fossa ovalis, a procedure first suggested as a means of preventing recurrence by de Takáts.[2]

Since 1930 my associates and I have endeavored to persuade patients who seek relief from varicosities for other than cosmetic reasons (a number of women with small single dilated veins apparent through sheer hosiery seek cosmetic relief only) to have high ligation of the saphenous vein with injection and thrombosis of the veins distal to the point of ligation.

The patients chosen for the combined ligation and injection had tortuous, moderate to large varicosities, and with one exception each

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1. Howard, Nelson J.: Jackson, C. R., and Mahon, E. J.: Recurrence of Varicose Veins Following Injection, Arch. Surg. **22**:353 (March) 1931.

2. de Takáts, Géza: Ambulatory Ligation of the Saphenous Vein, J. A. M. A. **94**:1194 (April 19) 1930.

patient suffered from symptoms directly attributable to the varicose state. The exception was a woman of 29 whose varicosities became apparent at the age of 14 and grew progressively larger until the distended veins became a distressing sight, although they produced no symptoms. Before proceeding with the ligation and injection, each patient underwent a thorough general physical examination; the blood pressure, urinalysis, differential white blood cell count and hemoglobin determination were recorded, and blood was taken for a Wassermann test. As in the previous study of treatment by injection alone, particular information with regard to the varicose veins was recorded on a separate chart. The position of the varices, their relative size and the competency of the valves of the saphenous and perforating veins were determined by the Trendelenburg and walking tourniquet tests. In instances in which the patency of the deep veins was questionable, tight pressure bandages worn for a week with relief afforded adequate evidence of patency in the deep veins of the leg.

METHOD

Previous to ligation the course of the saphenous vein, if not visible in the upper part of the thigh, was traced to the region of the fossa ovalis by palpation of the impulse transmitted on percussion. Under local anesthesia and through a transverse incision at the selected site of operation the saphenous vein was exposed and freed of surrounding areolar tissue. Unnecessary trauma to the vein was avoided. The vein was doubly ligated with ligatures of medium black silk, placed about 1 cm. apart. The ligatures were left long, so that after cutting between them they might be used as traction sutures. The proximal stump was transfixed and tied distal to the ligature, for it was evident from observations made at operation that coughing or increasing intra-abdominal tension markedly ballooned out the freed proximal stump. The respiratory venous excursions were readily observed. Failure to transfix as well as to ligate the proximal stump almost caused a fatality in one case. The ligature blew off under exertion and, following the resultant hemorrhage, the patient had a pulmonary embolus. It is important to tie and transfix the proximal stump without trauma from clamps or forceps that might lead to a propagated thrombus of the proximal stump. With the distal stump of the saphenous vein held taut by means of the long ligature, from 10 to 20 cc. of 20 per cent solution of sodium chloride was injected in a centrifugal direction. The vein was again tied to prevent the escape of the hypertonic solution into the tissues, and the wound was closed with interrupted sutures of fine black silk in the subcutaneous tissues and the edges of the skin and covered with sterile dressings. I have found it advisable to flush the wound with physiologic solution of sodium chloride before closure, immediately after injection of the sclerosing agent. Frequent postoperative inspections of the wound and dressings are necessary, for it is difficult to maintain dressings satisfactorily in the region of the groin, especially when the patient is ambulant. Sutures of the skin were removed in from five to seven days.

This procedure was carried out in the outpatient clinic by resident members of the surgical house staff. The patients were all ambulatory, and returned to their work or to their homes the day of the operation. It was usual to wait for the healing of the wound and removal of the stitches in the skin before proceeding to obliterate the remaining patent veins by injection of the thrombosing solution.

Injections were continued until all visible and palpable superficial veins were well thrombosed. Several instances of almost complete thrombosis of veins distal to the ligation occurred following the single injection, but in only one case was it so complete as to render further injections unnecessary. Patients with varicose ulcers were first treated by injection and application of a boot of Unna's paste until the small ulcers had healed or the larger ulcers were relatively clean and free from inflammation in the surrounding tissues before the ligation and further injections were attempted.

From May 1930 to February 1932, ninety-one ligations and injections were done on 68 patients in the outpatient clinic. Twenty-three of the ligations were bilateral. We were able to reexamine and question as to symptoms 58 patients, of whom 21 had both saphenous veins ligated. Since each set of varicosities is liable to recanalization and reproduction of signs or symptoms, it might be well for statistical purposes to list the observations by ligations rather than by patient. From this standpoint 86.8 per cent of the results were reexamined a year or

TABLE 1.—*Classification of Results of Treatment According to Appearance of Symptoms and Signs*

Classification	Recanalization	Percentage
—0	Complete recurrence to original size	3
—1	Visible as varicosities smaller than original	20
—2	Visible straight veins or visible isolated segments	37
—3	Not visible; palpable and percussable as patent; blood easily withdrawn from lumen	39
—4	Not visible; barely palpable as patent; aspiration of blood necessary to prove recanalization	1

more after ligation and thrombosis by injection. We were able to demonstrate recanalization in 100 per cent. The patency of the lumen of the vein is easily demonstrated by the transmission of a palpable impulse along the vein on percussion with the finger, and a Luer syringe with an intravenous needle serves to withdraw blood easily from the lumen of the vein.

The recanalization of the veins does not mean that the veins have recurred as varicosities. From the beginning of the following study the results were classified, on reexamination of the patient, in the following manner: —0, complete recanalization of the veins and recurrence of the varicosities to the original size; —1, the veins completely recanalized and visible as definite varicosities, yet smaller than the original veins; —2, visible straight veins, or isolated visible varicose segments and the varicose system as a whole recanalized, as shown by the aforementioned tests; —3, the original thrombosed varicosities not visible, but palpable and percussable as patent, and proved recanalized by the withdrawal of blood from the lumen with a syringe and needle; —4, barely palpable and percussable as patent but needing the final proof of withdrawal of blood from the lumen of the vein to prove recanalization. In table 1 the end-results are summarized in the foregoing manner. It is apparent

that only 23 per cent of the patients (those in classes —0 and —1) have recanalization to the point of recurrent varicosities, and 77 per cent (classes —2, —3 and —4) are to be regarded from a cosmetic standpoint as cured at the time of reexamination. The patients in class —2 may return for reinjection of the visible vein segment. In my experience young women with such a result returned for rethrombosis of the recanalized visible vein.

Fourteen patients received quinine and ethyl carbamate (urethane) as the sclerosing agent. The results in 12 patients were no more efficient and lasting than in patients treated with 20 per cent sodium chloride. Three patients received injections of sodium morrhuate in addition to the ligation of the vein. If the experience of the clinic were confined to these patients alone, we would not be justified in drawing conclusions as to the effectiveness of quinine and ethyl carbamate or sodium morrhuate. These solutions were used at intervals to the exclusion of treatment

TABLE 2.—*Symptoms and Signs Due to Varicose State After One Year*

	Before Treatment	One Year After Treatment
Pain	63	3
Fatigue	65	6
Burning sensation	38	0
Hemorrhage	4	0
Ulceration	25	2
Swelling and edema	44	3
Eczema	15	1
Cramps	4	2

with sodium chloride in patients who received injections without ligation. A sufficient number of such patients has been observed to suggest that the efficiency of thrombosis and the duration of results are certainly not superior to those noted following the injection of hypertonic saline solution. However, they have the advantage of not causing cramps during injection.

The symptoms and signs caused by the varicose condition in this series of patients before treatment are shown in table 2. Fatigue of the lower limbs, especially on long standing, was the most frequent complaint. This condition was present in 65 patients. A dull aching pain producing discomfort was present in 63. This was distinguished from a burning sensation, present in 38 cases. Definite severe cramps in the legs, not associated with exercise, came on while at rest or during the night in 4 people. Swelling and edema of the leg and ankle were noticed in 44 cases. There were twenty-five varicose ulcers, and 4 patients had spontaneous hemorrhage. Marked pigmentation of the lower part of the leg was present in 34 patients, and in 15 an eczematous, weeping cutaneous surface was an added complication.

On follow-up examination only 12 patients complained of symptoms. Six were still prone to fatigue of the legs on long standing; 3 com-

plained of pain, and 3 still had edema of the affected leg. Two had recurrence of cramps in the legs. In 1 patient the eczematous condition had never disappeared, and a small ulcer which had been healed recurred. Another patient in whom beginning recanalization of the veins had been noted at ten months had recurrence of an ulcer at twenty-one months, although the veins were classed only as —3. Only 1 patient with bilateral ulcers in the entire group with ulcer could not be reexamined a year following treatment. Thus there are 2 known recurrences among 25 patients treated for ulcers, 23 of whom were followed up for over a year after healing. This is particularly striking, for the patients with ulcers were not requested to wear pressure bandages or elastic stockings after ligation with thrombosis of the varicosities and healing of the ulcer.

As the patient is not aware of the reopening of the lumen in the veins, one has no means of estimating the time which elapses after treatment before recanalization occurs. However, in 4 patients recanalization was noted as beginning in four months, becoming complete at seven, eleven, twelve and sixteen months as —2, —2, —3 and —3 types, respectively, of recanalization. Two patients had a definite —2 grade of recanalization at five months. In 58, or in 65.8 per cent, recanalization was noted within the first twelve months after thrombosis. In the remaining 34.1 per cent recanalization was found in the second year after treatment. No definite correlation could be found between the grade of recanalization and the number of months elapsing from the time of thrombosis. One surprising fact noted in 13 patients, reexamined after the onset of recanalization at intervals of from four to fifteen months, was the failure of the veins to recanalize to such an extent as to change the classification of their grade of recanalization.

In the previous study of the end-results from injection alone the suggestion was made that "stripping" of the saphenous veins from the femoral opening to the knee, combined with thrombosing injections into the veins of the leg might prove a more permanent means of interrupting venous back pressure and preventing or retarding the recanalizing process. Four patients consented to enter the hospital for this operation. Of the 4, 1 stopped coming to the clinic for injections after discharge from the hospital, and could not be traced for follow-up examination. In the 3 remaining patients recanalization occurred to —2, —3 and —2 in eight and one-half, eleven and one-half and eleven months, respectively. The last case, that of a barber, was particularly interesting. First treated by injection and thrombosis in March 1928, his veins had recanalized to the —2 degree in six and one-half months. Again the treatment by injection produced excellent, rapid and complete thrombosis of all superficial veins from the ankle to the saphenous opening. Each time the thrombosing process was accompanied by fairly extensive perivenous inflammation, and there

can be no question as to the completeness of the thrombosis. In seventeen months the veins had again recanalized and this time they were as large as before any treatment, a —0 result, accompanied by tiredness, aching of the legs and recurrence of an ulcer healed for almost two years. A stripping operation was performed in the hospital during May 1930, at which time the veins below were completely thrombosed by injection. Perivenous inflammation in both calves again was marked, accompanied by tenderness and local induration along the channel left by the stripped vessels. In eleven months recanalization of the thrombosed vessels to the —2 degree had occurred, and a new vein had formed in the thigh from the saphenous opening to the region of the popliteal fossa. At operation the saphenous vein and the superficial circumflex iliac, superficial epigastric and superficial external pudendal veins, all tributaries at the saphenous opening, had been ligated and cut across.

The most serious complication that occurred in this operative series was a nonfatal pulmonary embolism in the patient referred to in the description of the technic of ligation, whose proximal saphenous stump was not transfixed as well as tied for additional security. This patient climbed four flights of stairs, and, under this exertion, the ligature blew off. The patient fainted from loss of blood and was taken to the city emergency hospital where a pressure pack bandage was applied. Secondary bleeding occurred and the patient later experienced a sudden thoracic pain followed by bloody expectoration and pleural pain with a friction rub. Rest in bed and careful nursing probably prevented the occurrence of a more serious embolic phenomenon.

CONCLUSIONS AND COMMENT

This experience is a blow to the hopes that ligation with injection might prevent recanalization of the thrombosed veins, or prevent recanalization to the extent of recurrence of the varicose veins. While recanalization could be demonstrated in 100 per cent of the patients reexamined from twelve to twenty-four months after treatment, it is particularly encouraging that in only 23 per cent had the condition advanced to the point of return of visible dilated veins or varicosities, and 77 per cent might still be considered cured from a cosmetic standpoint. Symptoms remained or recurred in only 12 patients, or 15 per cent of those reexamined. The treatment has been particularly effective in persons with ulceration or with the varicose type of eczema. Two ulcers recurred, and 1 patient (with an ulcer) failed to be relieved of the eczematous condition of the skin. Thirteen patients were followed up from four to fifteen months after recanalization had occurred. The recanalization did not progress to continued enlargement of the lumen of the vein. This is in marked contrast to my

experience with injection alone, for when recanalization was present, reinjection was considered necessary within from two to six months.

The 4 patients on whom the stripping operation and injection were done did not show better results than those with ligation and injection, and since the operative trauma is greater and hospitalization and general anesthesia are necessary, this method cannot be recommended or advised unless one completes the radical operation by excision of the saphenous system below the lowest stripped segment.

Wherever systematic follow-up studies have been carried out, based on personal reexamination rather than on returns from questionnaires, the results are in close agreement as to the return of varicosities following adequate thrombosis by injection, as well as in the observation that such return is not necessarily followed immediately by subjective symptoms. Outstanding among such follow-up observations are those of Svend Hansen, of Karsten Kettel and of Faxon. In 107 patients with uncomplicated varicose veins, Svend Hansen [3] reported good results in 35 per cent, with recurrence in 49 per cent and no improvement in 16 per cent from one to three years after treatment. The observations of Kettel [4] were particularly striking since they were carried out on a relatively large group of follow-up examinations (225) over a longer time (one to five years) than other reported results. He found that after one year 91.5 per cent of his patients with uncomplicated varicosities were free from symptoms (94.5 per cent free at the completion of treatment), and one third of the group reexamined had recurrences of varicosities. The percentage of recanalization was not observed. Kettel further found that as time elapses the number of patients without symptoms decreases. Thus, at the end of five years following treatment only 13 (28 per cent) of 45 patients examined had remained free of symptoms; 15 (33 per cent) were still improved and in 17 (38 per cent) the results were considered poor. These figures are for subjective findings. As to the objective return of varicose veins or complications Kettel classified the results as good, improved or poor. With this classification and considering both the "improved" and the "poor" results as showing objective evidence of the return of varicosities or dilated visible veins the incidence of recurrence for the five years of observation of uncomplicated varicose veins thrombosed by injection is as follows: first year, 38.5 per cent; second year, 65.6; third year, 64.8 per cent; fourth year, 79.5 per cent, and fifth year, 86.6 per cent. The group of patients whose varicosities were complicated by ulceration or eczema (131 with ulcers and 8 with eczema) offered the crucial test for the effi-

3. Hansen, Svend: Injektionsbehandlung von Varicen und ihre Resultate, Arch. f. klin. Chir. **166**:527, 1931.

4. Kettel, Karsten: Zur Injektionstherapie der Krampfadern: Augenblickliche Resultate; Nachuntersuchungen, Beitr. z. klin. Chir. **154**:585, 1932.

ciency and permanency of the treatment by injection. Of these 139 cases, Kettel was able to follow up 102. At the completion of the treatment 72 of the ulcers were healed, 9 were smaller and 13 uninfluenced by the therapy. Of the 72 healed ulcers 52 had remained healed when examined from one to five years after treatment, but 9 patients found it necessary to wear compression bandages, for otherwise the skin tended to break down. Thus, 43 of the 72 patients were able, from one to five years after treatment, to continue their usual occupations unhampered by compressive bandages or the necessity of continuous medical treatment for chronic ulcers of the legs. Of the 8 patients with varicose eczema only 1 was healed, 1 improved and 6 showed no change in their condition over a three year period of observation.

Every physician has the memory from student days of patients with ulcers of the leg older than the student, the wounds having been dressed by a continuous succession of interns, house officers and residents beyond the memory of the oldest physician of the clinic. With such memories the results of Kettel are in overwhelming contrast.

Faxon,[5] at the Massachusetts General Hospital, followed approximately half of 613 patients treated by injection. In a careful and candid survey of the results at an average of one and one-fourth years after the completion of treatment, he found that there were recurrences of varicose veins in 63 per cent of the 314 patients followed up. New varicosities developed in 25 per cent of the cases, which is higher than in my own experience and observations. The findings of Faxon also show that the patient's appreciation is often greater than the objective evidence warrants, for 59 per cent were enthusiastic, 34 per cent moderately pleased and only 7 per cent disappointed in the results. Of the patients having symptoms referable to the varicose state, 38 per cent were relieved of pain and 19 per cent of edema, and in 61 per cent the ulcers remained healed over the period of observation.

In the treatment by injection alone particular efforts were made to obtain permanent obliteration of the lumen of the vein by means of an efficient thrombosing agent (20 per cent solution of sodium chloride); and the following adjuncts: (1) thrombosis of the saphenous vein in the thigh (frequently ascending thrombosis to the saphenofemoral junction was secured); (2) emptying of the vein at the time of injection by elevation to or beyond the horizontal plane with stripping of the vein by means of the finger; (3) localization of the segment of the vein in which the injection was made by means of proximal and distal tourniquets; (4) pressure bandages during and after the period of thrombosis to achieve collapse and adherence of the walls of the veins; (5) hot solutions (110 F.) to add thermal to chemical trauma,

5. Faxon, Henry H.: End Results in the Injection Treatment of Varicose Veins, New England J. M. **208**:357 (Feb.) 1933.

and (6) mechanical trauma by rough massage along the vein following the injection. The blame for recanalization or recurrence has been placed, particularly by McPheeters,[6] on the failure to observe many of the adjuncts to injection.

Since from the beginning all efforts were aimed at permanent results as well as the immediate relief of the symptoms and complications of varicosities, I have utilized the factors enumerated to further the thrombosis and lasting organization of the sclerosed veins. In spite of this, the vein responded with recanalization, the natural history of a thrombus, and, as these follow-up studies have shown, such recanalization proceeds to the extent that the varicosities recur, and the symptoms of the disease are eventually manifest. Undoubtedly this will be true of the treatment by ligation and injection as well, for my figures show the return of varicosities from this procedure within the short time of observation. I have reason to believe that this return will be slower and the development of the varicose veins and their symptoms may remain in abeyance for a longer period than with injection alone. One discrepancy between my results and those of other observers might well be explained by the fact that in the first report patients were classed as having recurrences even though the recanalized veins had not become dilated varicosities. The suggestion of Dr. Emile Holman, that recanalization should not be considered necessarily as a recurrence, is valuable, and particular attention was paid to it in the reexamination of patients in the present series. McPheeters,[7] too, showed that recanalization does not progress with equal rapidity along the entire course of the lumen of the vein, and that even in the presence of recanalization the actual condition may still be similar to multiple ligations along the course of the saphenous system. De Takáts'[8] most recent report gave only 10 per cent recurrence following treatment by ligation and injection. I feel that his admitted and pardonable failure to secure the return of the patients from the clinic for reexamination as well as the interest we have manifested in the process of recanalization explains the gross differences in the two findings.

The problem of the treatment of varicose disease has been advanced tremendously by the adoption of treatment by injection. Few physicians now consider returning to the radical operation. The purpose of evaluation of treatment by injection is not to discourage or to abandon the distinctly valuable therapeutic method, but to find its

6. McPheeters, H. O.; Merkert, C. E., and Lundblad, R. A.: Causes of Failure in Injection Treatment of Varicose Veins, J. A. M. A. **96**:1114 (April) 1931.

7. McPheeters, H. O., and Lufkin, N. H.: Pathological Study of Injected Varicose Veins, Surg. Gynec. & Obst. **54**:511, 1932.

8. de Takáts, Géza, and Quillin, Lawrence: Ligation of the Saphenous Vein, Arch. Surg. **26**:72 (Jan.) 1933.

limitations. The next step should be prophylactic. All varicose veins do not have a common cause. In over one third of the patients the first signs of varicosities develop in adolescent or early adult years. This group seems to have a congenital origin, and studies of the embryologic development of the valves of the veins of the extremities and of the progressive disappearance of many or all the valves in the saphenous system in the first few months of extra-uterine life suggest a clue to the development of this presumably congenital group. Endocrine factors have been mentioned, but no one has satisfactorily indicated the endocrine disturbance or separated it clearly from those of mechanical nature. It is known, however, that varicosities make their appearance following thrombophlebitis of infectious diseases, childbirth and operative procedures. Also, varicosities are known to have a definite relation to trauma of the lower extremities. Fractures, crushing injuries and osteomyelitis of the lower part of the leg are often followed by unilateral varicosities. During operative procedures for osteomyelitis or for the reduction of a fracture one may encounter thrombosed veins from which, on incision, fragments of dark thrombi may pour into the operative wound. Examination of legs amputated for crushing or infected compound injuries often reveals the venae comites as the source of interstitial hemorrhage or thrombosis far more frequently than the arteries. The posttraumatic edema of fractures of the lower part of the leg may persist for months, occasionally for two years after the removal of splints and the beginning of weight bearing.

The early and continued use of pressure bandages or elastic support of the limbs of patients with thrombophlebitis and edema is imperative whether the condition is puerperal, postoperative or traumatic.[9] Adequate support given the superficial saphenous venous system from the moment the patient is ambulatory not only prevents the increase of edema but should accelerate to the fullest extent the recanalization of the deep, thrombosed veins and in this way prevent or minimize the future development of varicosities in the superficial venous system.

In regard to operative ligation at or near the saphenofemoral junction followed by treatment by injection, my experience demonstrates that such a procedure does not prevent the recanalization of therapeutically thrombosed veins, but I feel that it definitely retards the

9. It is the custom of Dr. Emile Holman to insist that patients with postoperative thrombophlebitis remain in bed until the edema subsides. The ambulatory state is then not followed by edema. Repeated trials should be made to determine when freedom from edema (with the patient ambulatory) occurs. Three months in bed is not too long a time to carry out this regimen. A woman who had bilateral postoperative thrombophlebitis with marked edema was in bed for three months in order to arrive at the ambulant edema-free state. Five years subsequently she was free from edema, had no varicosities and was able to carry on her normal mode of living.

recurrence of the varicosities. Certainly persons with massive varicosities, with incompetence of both saphenous and perforating valves and with ulceration or eczema have benefited more by ligation than by injection alone. For uncomplicated varicosities without incompetent perforating veins and without ulceration or eczema, injection alone produces an eminently satisfactory result from the patient's point of view. That such injections will require repetition over the course of years should be explained to the patient and anticipated by the physician. Injection into varicosities for cosmetic reasons alone should be carried out in early varicosities, even in young adults, so as to reduce continually or to prevent the reflex flow and stagnation that are believed responsible for the complications of the varicose state. A possible danger in this might be that veins dilated early, when thrombosed, might suffer destruction or distortion of the competent valves by the subsequent organization, so that in time the system would lend itself with greater ease to dilation by hydrostatic pressure in the upright position. I have not found this to be true so far, and in patients with competent perforating valves with definite recurrence of varicosities after injection I have not observed incompetence of perforating veins on return of the varicosities.

SUMMARY

1. Eighty six and eight-tenths per cent of the patients treated by ligation and injection were observed for from a year to twenty-nine months after treatment.

2. In spite of the ligation and injection, 100 per cent of these patients showed recanalization of the previously thrombosed veins.

3. In only 23 per cent was there recanalization to the extent of the return of varicosities or of visible large veins; 77 per cent of the patients could be considered cosmetically cured.

4. At the end of the period of observation symptoms remained or recurred in only 12 patients—15 per cent of those followed up or 13 per cent of the entire group treated.

5. Ligation with thrombosis by injection cannot prevent recanalization, but it retards recanalization to the point of return of varicosities, and should be used in complicated varicosities (incompetent perforating veins, ulcers and eczema).

6. Prophylaxis of varicosities should be the aim of the physician. Prolonged use of pressure bandages or elastic support should be insisted on in every case of thrombophlebitis or edema of a local circulatory nature in the lower extremities. Early uncomplicated varicosities should be treated by thrombosis by injection, repeated when recurrence of varicosities takes place in order to guard against the complications of the untreated varicose state.

THYROID DISORDERS

VI. THE SUPRARENAL FACTOR IN REACTIONS TO THYROIDECTOMY

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Many of the reactions characterizing the various effects of operation on patients with hyperthyroidism resemble the responses which can be produced in such patients by the subcutaneous injection of epinephrine hydrochloride. As a result of clinical studies made during the past year, which are reported here, the belief seems warranted that the suprarenal glands play an important rôle in the clinical manifestations exhibited by patients with hyperthyroidism before and during thyroidectomy. Cannon and his associates [1] showed by physiologic experiments that the secretion of the thyroid and the active iodine-containing compound isolated from the thyroid gland by Kendall [1b] sensitized the sympathetic nervous system to the action of epinephrine. These researches explain the increased sensitiveness to epinephrine exhibited by patients suffering with hyperthyroidism and form the basis of the epinephrine test (E. G.[2]).

Long experience in observing the responses produced by the subcutaneous administration of epinephrine hydrochloride in patients with hyperthyroidism has made us familiar with the symptoms and signs which are manifested whenever there is a sudden increase in the amount of epinephrine introduced into the circulation. Thus in the epinephrine test described by one of us (E. G.) it was found that when a dose of 0.5 cc. of 1:1,000 solution of epinephrine is injected subcutaneously into the patient with hyperthyroidism, the following signs and symptoms are produced. There occurs an early, fairly sharp rise of the systolic blood pressure and pulse rate of from 10 to 50 or more points. At the same time one finds as a rule a slight to moderate fall of the diastolic

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Read before the American Association for the Study of Goitre, Memphis, Tenn., May 17, 1933.

1. (*a*) Cannon, W. B., and Cattell, McK.: Studies on the Conditions of Activity in Endocrine Glands: III. The Influence of Adrenal Secretion on the Thyroid, Am. J. Physiol. **41**:74, 1916. (*b*) Levy, R. L.: IV. The Effect of Thyroid Secretion on the Pressor Action of Adrenin, ibid. **41**:492, 1916.

2. Goetsch, E.: Newer Methods in the Diagnosis of Thyroid Disorders: Pathological and Clinical: B. Adrenaline Hypersensitiveness in Clinical States of Hyperthyroidism, New York State J. Med. **18**:259, 1918.

pressure. As a result, the pulse pressure, which is indicative of the work of the heart, is greatly increased. In the course of from thirty to thirty-five minutes there is a moderate fall in the systolic pressure, then a moderate secondary rise, which is succeeded by a gradual fall to the normal in about one and one-half hours. The diastolic pressure also returns to its previous level in this interval. The respirations become deeper and often moderately accelerated. Simultaneously with these changes one sees an exaggeration of the clinical picture of exophthalmic goiter or hyperthyroidism, especially the nervous manifestations. All or part of the following symptoms are to be found: increased tremor, apprehension, precordial and peripheral throbbing, and asthenia, and, in fact, an increase of any of the symptoms of which the patient may previously have complained. Vasomotor changes may be present. The initial vasoconstriction with pallor and coldness of the hands and feet is followed by vasodilatation with flushing and sweating. There may be a slight rise in temperature and a slight diuresis. Furthermore, in the past several years studies conducted in the surgical clinic of the Long Island College Hospital have shown that a striking leukocytosis occurs promptly after the subcutaneous injection of epinephrine hydrochloride in the patient with hyperthyroidism. In a paper on this subject, read before this association two years ago by one of us (E. G.), it was pointed out that the hypodermic injection of 0.5 cc. of epinephrine hydrochloride in a patient with hyperthyroidism was followed by a prompt and sharp increase in the number of leukocytes. These may increase from the normal count to 30,000 or 35,000 per cubic millimeter of blood. The differential count at this time indicated a striking mononucleosis in which there were both relative and absolute increases in the mononuclear cells. Simultaneously there occurred a striking diminution in the percentage of polymorphonuclear cells. At the end of from one to two hours, the white cell count had returned approximately to the preinjection level. Apropos of this, Menkin [3] pointed out that emotional stimulation in animals caused a relative increase in the mononuclears in the circulating blood. An increase in the blood sugar is also known to occur following an injection of epinephrine hydrochloride, which presumably mobilizes the glycogen in the body tissues. Incidentally, a concomitant rise in the body temperature has been noted.

Bearing in mind these various manifestations produced by the administration of epinephrine hydrochloride in the patient with hyperthyroidism, the surgeon experienced in operations on the thyroid gland could not fail to be impressed by a striking similarity in the clinical reactions of the patient with hyperthyroidism to thyroidectomy and to the admin-

3. Menkin, V.: Emotional Relative Mononucleosis, Am. J. Physiol. **85**:489, 1928.

istration of epinephrine hydrochloride. Accordingly, we planned to study more minutely the various effects produced by thyroidectomy. Before describing in detail the operative reactions, we shall enumerate the harmful factors which are inherent in practically every major operation and which are directly or indirectly responsible for these reactions. These factors are well recognized. They are, in brief, the emotional states of fear and apprehension and the exhausting factors of pain, trauma, possible hemorrhage, metabolic and nervous strain, anesthesia and the possible anxiety, nausea, vomiting and starvation of the immediate postoperative period. It is needless to elaborate further on the nature of the major ordeal of operation, particularly on a nervous and sensitive patient. In this connection one may recollect the interesting and significant contribution of Cannon [4] with respect to the function of the suprarenal glands and their increased activity resulting from the emotions of fear and anger and following painful stimuli. There was produced accordingly an increased amount of epinephrine in the organism. Thereupon he elaborated his theory of the emergency function of the suprarenal medulla in pain and the major emotions. Surgeons are forever indebted to Crile [5] for emphasizing these noxious factors and for his technical methods of reducing their harmful effects in all operations and particularly in operations on the sensitive patient with hyperthyroidism. His technic of anoci-association has been fully described and is familiar to all.

It is our purpose to describe somewhat minutely the reactions to thyroidectomy observed in the patient with hyperthyroidism, to point out the similarity of these reactions to those previously exhibited by the same patient after a hypodermic injection of epinephrine hydrochloride and to offer what appears to be demonstrable evidence that suprarenal activity is the causative agent in the production of the characteristic operative reactions to thyroidectomy.

METHOD OF STUDY

The preparation of the patient and anesthesia were uniform. It has been customary to administer 1/6 grain (0.0108 Gm.) of morphine hypodermically an hour before operation and a second injection of 1/8 grain (0.0081 Gm.) thirty or forty minutes later. The anesthetic used in all the cases consisted of nitrous oxide and oxygen supplemented occasionally with small amounts of ether. This was administered by an anesthetist of many years' experience. The factor of anesthesia was thus constant in all the studies. In a considerable number of control operations such as excision of tuberculous glands of the neck, herniotomy

4. Cannon, W. B.: The Emergency Theory of the Adrenal Medulla in Pain and the Major Emotions, Am. J. Physiol. **33**:356, 1914.

5. Crile, G. W.: Protection of the Patient in Surgery on the Thyroid., Surg., Gynec. & Obst. **32**:213, 1921; The Present Status of Anociation: A Critical Review, Ann. Surg. **86**:251, 1927.

and simple appendectomy it was noted that nitrous oxide alone produced little change in the pulse rate, blood pressure or respiration. Patients were protected in every ordinary way, but it was not possible to carry out the minute details of anoci-association observed by Crile. However, we are confining ourselves to interpretation and explanation of the operative reactions themselves, rather than offering means of combating them.

In a small series of recent cases carefully studied, the following routine was adopted: On the morning of operation, observations were made on the pulse rate, blood pressure and temperature. Samples of blood were taken for blood counts and blood sugar determinations. The preliminary injection of morphine had been given, and the same observations were repeated on the arrival of the patient in the operating room and again immediately before the anesthetic was begun. Similarly, observations were made at intervals during the operation and during the immediate postoperative period and, in some instances, at various times during the forty-eight hours or more after operation. The findings following operation are interesting but are not included in this preliminary report.

REPORT OF CASES

CASE 1.—*Clinical Behavior of a Patient with a Highly Toxic Exophthalmic Goiter Before, During and After Thyroidectomy.*

History.—Miss A., representative of the group of young persons suffering with highly toxic hyperthyroidism resulting from exophthalmic goiter, was 24 years of age and had had progressive hyperthyroidism over a period of one year. The thyroid gland was definitely enlarged and showed marked vascularity. Her eyes were strikingly prominent, and there had been a great loss of weight. The pulse rate varied between 120 and 130. After ten days of preparatory treatment with iodine, the pulse rate diminished to 110. The basal metabolic rate before this period was plus 52.9 per cent, and following the ten days of treatment with compound solution of iodine it fell to only plus 45 per cent, and the clinical improvement was not marked. Four days later the patient was operated on. At this time it was not considered safe to do more than a right hemithyroidectomy, which was performed at 10:30 a. m. on April 14, 1933.

Preoperative Period.—The patient was reasonably calm while in her room. Unfortunately, there was a delay in the operating room before the anesthetic was administered. The patient became restless; her face was flushed, and, as a result of this period of waiting, there was a definite rise in the pulse rate and also in the rectal temperature. The respirations and the blood sugar were also increased. This is a known response to emotion, particularly fear and apprehension. There was a slight fall in the blood pressure, which might be attributable to the moderate dose of morphine. There was as yet no decided change in the total white blood count or in the differential count. The rectal temperature rose 0.4 F. during this period. At the same time the pulse rate rose from 108 to 135. There was a slight diminution in the total leukocyte count, with a relative rise in the polymorphonuclears and a fall in the mononuclears. The systolic blood pressure fell slightly, but there was a rather definite fall in the diastolic pressure, thus increasing the pulse pressure even before the anesthetic was begun.

Operative Period.—Immediately before and more particularly immediately after anesthesia was begun, we found a decided change in all the reactions. The behavior of each reaction up to its maximum, which appears in about from twenty-five to thirty-five minutes after the beginning of the anesthesia and the operation, is given.

Pulse: The pulse rate rose from 144 to 180, an increase of 36 points, and during a short period it reached 190, but we did not attribute these 10 points to the operative procedure per se, because there was slight pressure momentarily on the trachea during the delivery of the lobe. Throughout the operation there was no other embarrassing factor of this character, the anesthesia being satisfactory. There occurred an increase in the pulse rate of 72 points from the normal of 108 when the patient was in her room to 180 at the peak of the reaction.

Blood Pressure: The systolic blood pressure dropped from the preoperative level of 140 mm. to 124 mm. of mercury and then rose to a peak of 176 mm. Simultaneously, the diastolic pressure was maintained at the low level of about 65. Accordingly, the pulse pressure was increased from the preoperative normal of 50 to 108, an increase of 58 at the height of the reaction.

Leukocytes: There was a striking increase of 10,400 in the total white cell count, namely, from 7,250 to 17,650 at the peak of the reaction. The count had thus more than doubled.

Differential Blood Count: The polymorphonuclear leukocytes, which showed a slight rise up to the time the anesthesia was begun, immediately and precipitously fell from 63 per cent to 34 per cent just after the peak of the reaction. The mononuclear leukocytes, which showed a preliminary slight fall, rose precipitously during this interval to 66 per cent. Thus, the differential picture before operation was reversed during operation.

Blood Sugar: Furthermore, there occurred a moderate rise of the blood sugar from 80 mg. per hundred cubic centimeters of blood, while the patient was in her room, to 95 mg. just prior to administration of the anesthetic. Following this there was a definite increase to 120 mg. just after the peak of the reaction. There was thus an increase of 40 mg. in the blood sugar.

Rectal Temperature: During all this time the rectal temperature rose from 98.8 F., when the patient was in her room, to 101.2 F. at the peak of the reaction, namely, an increase of 2.4 F.

After the peak of the reaction had passed there was a gradual tendency to a restoration of the previous preoperative picture, although all the factors did not behave in the same way.

Period of Subsidence of Reactions.—The operative reactions after the peak had been reached and during the postoperative period to 5:30 p. m., seven hours after operation, were studied next.

Pulse: The pulse rate gradually fell from the peak of 180 during operation to 158 at the end of operation, and to 118 in the evening.

Blood Pressure. The systolic blood pressure fell less strikingly, from 176 at the peak to 156 at the end of the operation, and then gradually diminished to 146 in the evening, thus remaining slightly above the preoperative normal pressure, which was 140.

The diastolic pressure rose from its low point of 60 at the peak of the operation to 70 at the end of the operation, and then gradually increased to 90 in the evening. Thus, the pulse pressure, which was much increased from 50 before operation to 108 during the operation, had returned to 50 or to the preoperative normal by evening.

Leukocytes: The total white cell count behaved in a strikingly opposite manner; that is, while the remaining operative reactions were tending to return to the preoperative normal the leukocytes continued to increase. Thus the peak of 17,650 was maintained practically to the end of the operation. During the postoperative period there was a further increase to 26,600 as compared with a preoperative

normal of 7,250. This occurred about one and one-half hours after the completion of the operation, and in the evening the white cell count was still high, namely, 19,250. The postoperative rise in the white cell count has been previously observed and reported by Meleney.[6] We believe that this increase in the white cells, largely of polymorphonuclear type, is a reaction to trauma and serum absorption, and not to the suprarenal factor.

Differential Blood Count: The mononuclear count following the peak of the reaction fell precipitously from 66 to 33 per cent at the end of the operation, and finally dropped to 13 per cent at 5:30 p. m. Conversely, the polymorphonuclear count rose abruptly from its low point of 34 per cent during the operation to 47 per cent at the end of the operation and to 87 per cent at 5:30 p. m. Thus, in chart 1 there is a crossing of the lines twice as a result of the changes in the differential count, the polymorphonuclears showing a definite decrease in number during the operation and a marked rise much above their normal level at the end of the operation. The reverse holds true with reference to the mononuclears, which show a definite rise during the operation and a precipitous fall to 13 per cent in the evening.

Blood Sugar: The blood sugar level was maintained at its high operative level of from 120 to 125 mg. per cubic centimeter of blood during the subsequent two and one-half hours. Further determinations were not made in order to avoid disturbing the patient by puncture of a vein.

Rectal Temperature: The temperature gradually fell from its highest point during operation, 101.4 F., to 99.6 F. in the evening.

There was a definite and positive reaction on the part of the patient subjectively and particularly objectively. We have described these operative reactions in detail in order to compare them with the similar reactions observed four days previously in the same patient after the hypodermic administration of 0.5 cc. of 1:1,000 solution of epinephrine. In general, there is a striking parallelism, in the reactions to operation and to epinephrine, as is well illustrated in charts 1 and 2. The differences are those of degree rather than character, the operation in this case causing a more definite response than is brought out by the injection of 0.5 cc. of epinephrine hydrochloride.

Clinical Response to the Injection of Epinephrine Hydrochloride.—The response to the injection of 0.5 cc. of 1:1,000 solution of epinephrine (chart 2) given on April 11, three days before this patient was subjected to thyroidectomy, follows. Observations similar to those which were made at the time of operation and which have been described had been previously made in a study of the clinical response of this patient to the hypodermic injection of epinephrine hydrochloride. The patient's normal was established in regard to the various observations which we intended to make. These observations were then further continued after the injection of the epinephrine hydrocholride. The patient was relatively calm and composed during the preinjection period. A summary of the reactions is given here (chart 2).

Pulse: The preinjection pulse rate averaged 125. There was an abrupt rise to a peak of 178 in from five to ten minutes, an increase of 53 points. Thereupon the pulse showed a continual gradual fall to the preinjection level of 125; one hour after the injection and continuing for another half hour it fell to 120, or just below the preinjection level.

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6. Meleney, F. L.: A Study of Anteoperative and Postoperative Blood Counts in Noninfective Surgical Conditions, Ann. Surg. **67**:129, 1918.

Blood Pressure: The systolic blood pressure taken when the patient was resting quietly in bed was rather constant at 145 mm. of mercury. Immediately after the injection of epinephrine hydrochloride there was a precipitous rise which reached its peak at 198 in a period of eight minutes, an increase of 53 mm. of mercury. There was a fairly prompt fall to 156 in thirty-five minutes, and then a gradual fall to 132 in one and one-half hours following the injection, at which time the reaction had practically subsided. The diastolic pressure beginning at 68 rose sharply to 92 at the peak, at which time the pulse pressure had increased to 106, as compared with the preinjection pressure of 78. A definite

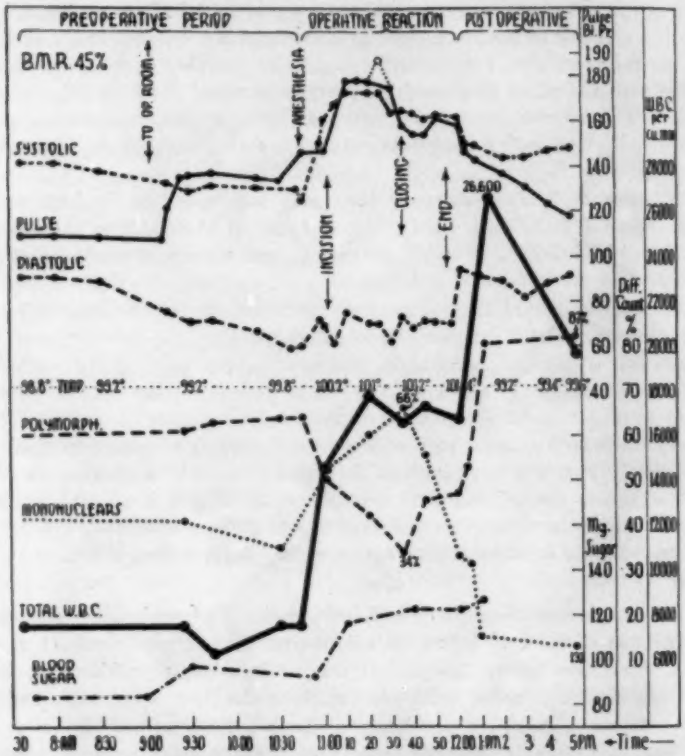

Chart 1 (case 1).—Clinical chart in a case in which right hemithyroidectomy was performed on April 14, 1933. The chart is divided into the preoperative, operative and postoperative periods, and shows graphically the striking changes which occur during these periods in the pulse rate, blood pressure, leukocytes, blood sugar and temperature in response to the operative procedure.

increase of pulse pressure was maintained over a considerable period following the injection of epinephrine hydrochloride and resulted largely from a continued fall of the diastolic pressure.

Leukocytes: The total white cell count rose from its preinjection level of 7,550 to 11,650 at its peak, an increase of 4,100 in about twenty minutes after the injection. The count then gradually fell at the end of one and one-half hours to 7,400, which was just below the preinjection level.

Differential Blood Count: The differential blood count showed striking changes. The preinjection percentage of the polymorphonuclears was 59; after the injection there was a precipitous fall to 42 per cent in twenty minutes, and then during the remainder of the period there was an abrupt rise after one and one-half hours to 72 per cent, namely 13 per cent above the preinjection level. The reverse was true of the mononuclears, which rose abruptly from a preinjection level of 41 per cent to 58 per cent in twenty minutes and then fell rather abruptly after one and one-half hours to the low of 28 per cent, about 13 per cent below

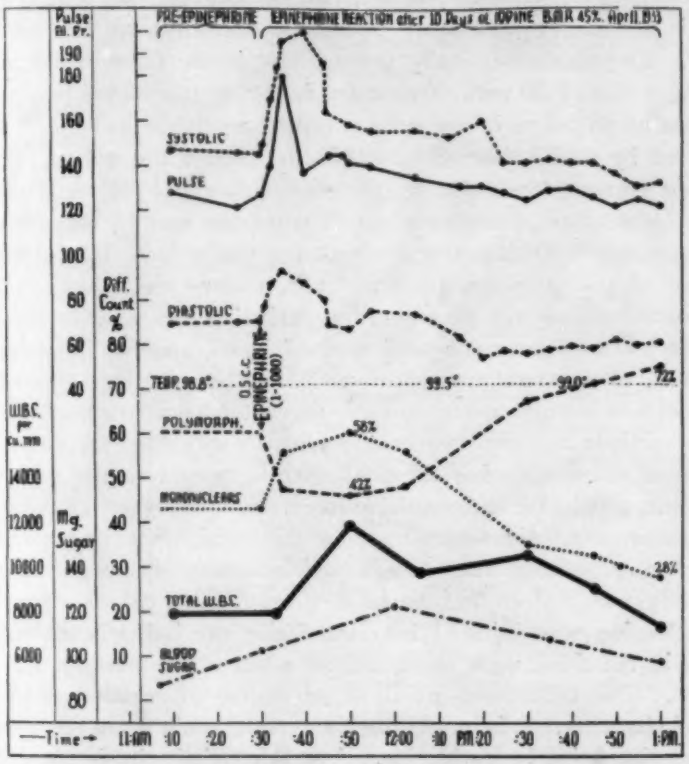

Chart 2 (case 1).—Clinical chart showing the changes which occur in the pulse rate, blood pressure, leukocytes, blood sugar and temperature in response to the subcutaneous injection of 0.5 cc. of 1:1,000 solution of epinephrine. These observations were made on April 11, 1933, three days before the hemithyroidectomy. A comparison of charts 1 and 2 shows a striking similarity in the clinical effects produced by operation and by the injection of epinephrine hydrochloride. The differences are merely of degree of response and not of general character.

the preinjection level. This behavior of the differential count is precisely like that found during operation.

Blood Sugar: The blood sugar rose from the preinjection level of 82 mg. per hundred cubic centimeters of blood to 100 mg. just before the injection of epinephrine hydrochloride, a finding which we attributed to emotion. A peak

of 120 mg. was reached about one-half hour after the injection. Following this, there was a gradual fall at the end of one and one-half hours to 95 mg., 13 mg. above the preinjection level.

Rectal Temperature: During the period before the injection of epinephrine hydrochloride, the rectal temperature registered 98.8 F.; forty minutes after the injection, the temperature rose to 99.1 F., and thirty minutes later it was still 99 F.

Comment.—A woman, aged 24, suffering from a highly toxic exophthalmic goiter, was subjected to a hemithyroidectomy under nitrous oxide-oxygen anesthesia. Characteristic clinical reactions were produced by this procedure, particularly during the operation, but also preoperatively. They included briefly a sharp rise in the pulse rate from 110 to 190, a rise of 36 mm. of mercury in the systolic blood pressure, an increase of 58 points in the pulse pressure, a marked leukocytosis characterized by an increase of 10,400 in the total white cell count and a striking mononucleosis during operation followed by a secondary fall in the percentage of mononuclears toward the end of the operation; synchronously with this there occurred a preliminary fall in the percentage of polymorphonuclears and a secondary rise which continued to increase during the postoperative period, an increase in the blood sugar of 40 mg. per cubic centimeter of blood, and finally an increase of 2.4 F. in the rectal temperature. After the maximum reaction had been reached during operation, there was a tendency to a restoration of these reactions to their preoperative normal, with the exception of the continued changes during the postoperative period in the total white cell count and in the differential picture.

Similar observations were made on the reactions in the same patient during an epinephrine test (table 1) carried out three days before operation. It was found that when a dose of 0.5 cc. of epinephrine hydrochloride was injected hypodermically precisely the same characteristic reactions were produced as when thyroidectomy was performed. The differences are those of degree of reaction and not of general character. It is unnecessary to enumerate in detail the responses to the epinephrine hydrochloride. A striking similarity is noted in the responses to operation and in those produced by the epinephrine in the same patient. This is well illustrated by reference to charts 1 and 2. The injection of a larger dose of epinephrine hydrochloride would doubtless duplicate the somewhat greater degree of reaction produced by operation, but this would not be justified. It might even be unsafe. We have good reason to believe, therefore, that epinephrine plays a large rôle in the production of the operative clinical picture. We have studied a number of cases of exophthalmic goiter of varying degrees of toxicity from the rather mild cases to those of moderate intensity, and briefly, the reactions both to operation and to epinephrine, as would be expected, are of a correspondingly less marked intensity. Similarly,

the reactions in patients with toxic adenoma are definitely less marked than those we have described in the case of exophthalmic goiter.

TABLE 1.—*Clinical Reactions to the Hypodermic Injection of Epinephrine Hydrochloride in Case 1*

Time	Pulse	Respiration	Blood Pressure	Blood Count	Comment
11:00	140	25	150/74	.....	General status, subjective relaxation; objectively patient is somewhat nervous and upset; precordial and neck pulsations are fairly prominent; fairly marked finger tremor; hands warm and mildly moist Blood sugar average before injection of epinephrine, 82 mg. per 100 cc. of blood
11:10	...	..	.....	.....	Temperature, 98.8 F.
11:10	126	27	146/68	W.B.C. 7,500 Pmn. 59% Mono. 41%	Status the same
11:24	120	26	145/68		
11:29	...	..	.....	.....	Specimen of blood taken (sugar, 100 mg. per 100 cc.)
11:31	...	..	148/76	.....	Injection of epinephrine hydrochloride (0.5 cc. of 1:1,000 solution)
11:32	138	..	168/84	.....	Feels weaker; "catching her breath"
11:34	...	30	186/90		
11:35	178	..	194/90	W.B.C. None Pmn. 46% Mono. 54%	Precordial throbbing; pallor of face; dyspnea; restless
11:39	134	26	199/86	.....	Slow, strong beats alternating with more rapid ones; precordial throbbing; tremor increased; hands dry and warmer; feels better
11:43	144	30	180/78	.....	Beats of equal force now; rate is regular and now stabilized
11:45	144	30	162/68	.....	Rate and depth of respiration increased; pallor disappearing; precordial and neck throbbing still present; not conscious of much disturbance; hand and finger tremor still marked; hands warm and dry
11:50	140	26	158/66	W.B.C. 11,650 Pmn. 42% Mono. 58%	Diminished clotting time, making smear taking difficult; feet feel warm
11:55	138	24	156/74	.....	Hands warm, slightly moist; feet slightly cool to palpation
12:00	...	..	.....	.....	Specimen of blood taken (sugar, 120 mg. per 100 cc.)
12:05	134	25	156/72	W.B.C. 9,650 Pmn. 43% Mono. 57%	Feels more relaxed and comfortable; moderate finger tremor still present
12:10	...	..	.....	.....	Rectal temperature, 99.1 F.
12:15	130	27	152/62	.....	Feels quite relaxed, comfortable; somewhat tired; finger tremor still present and moderate in degree; hands warm and dry; cardiac and neck pulsations still increased but moderate
12:20	130	25	158/52		
12:25	128	28	140/56	.....	Same status
12:30	126	25	140/54	W.B.C. 10,500 Pmn. 63% Mono. 37%	
12:35	128	25	142/56	.....	Specimen of blood taken (sugar, 105 mg. per 100 cc.)
12:40	128	25	140/58	.....	Rectal temperature, 99 F.
12:45	124	30	140/58	W.B.C. 8,670 Pmn. 69% Mono. 31%	Status generally the same; is now more comfortable; cardiac and neck pulsations about the same as before injection of epinephrine; hands warm, mildly moist
12:50	120	25	136/60		
12:55	124	25	130/58		
1:00	122	28	132/58	W.B.C. 7,400 Pmn. 72% Pmn. 72% Mono. 28%	Specimen of blood taken (sugar, 95 mg. per 100 cc.)

CASE 2.—*Clinical Behavior of a Patient with a Mildly Toxic Adenoma (Fetal) During the Preoperative, Operative and Postoperative Phases of Operation for Excision of Adenoma.*

History.—The patient, representative of the group of relatively young women suffering with mildly toxic adenoma of the so-called fetal type, was 29 years

of age. A small lump was noticed on the left side of her neck after the birth of her first child four years previously. Since first noticing the lump, she experienced slight nervousness, fatigue, emotionalism and irritability. Throbbing of the heart and tremor were not noted. There was an adenoma as large as a small lime in the left lobe of the thyroid gland. It was semifluctuant and produced a feeling of choking on pressure. The pulse rate was 100. The blood pressure was 104 systolic and 66 diastolic. The patient had lost 10 pounds (4.5 Kg.) during the previous four or five years, her present weight being 105 pounds (42.6 Kg.). Excision of the adenoma was done on April 5, 1933. The basal metabolic rate after the period of therapy with an iodine preparation was plus 5.9 per cent. There had been no appreciable change in the clinical status following the treatment with iodine.

Preoperative Period.—The patient was quiet and composed while in her room at 7:30 a. m. and at 8:00 a. m., at which time she was taken to the operating room. Small doses of morphine had been previously administered. As indicated in chart 3, the changes in the various factors of reaction during this preoperative period were either insignificant or negligible. There was a slight fall in the pulse rate and in the systolic blood pressure. There was no change in the diastolic pressure. There was also a slight diminution in the total white cell count. The differential count showed some changes, such as a slight fall in the percentage of polymorphonuclear leukocytes and a slight rise in the mononuclear cells. There was no change in the rectal temperature. Blood sugar determinations were not made in this case. In other words, the changes noted during the preoperative period were only slight and may be compared with the definite changes noted during the preoperative period in the patient with the toxic exophthalmic goiter previously described.

Operative Period.—Pulse: During the period of waiting in the operating room and until anesthesia was started, the rise in the pulse rate was the only really significant change noted. There was an increase from 90 to 120, a rise of 30 points. This compares with a rise of 72 points in the case of exophthalmic goiter under comparable conditions. Subsequently, after anesthesia was begun, the pulse rate rose from 120 to 132. Thereupon there was a temporary fall to 108, with a subsequent rise to 136 and then a gradual decline with oscillations to 120. In other words, there was no further increase in the pulse rate produced by the operation per se than was produced by the preoperative factors concerned. The high point of 132 compares with 190 plus in the case of exophthalmic goiter.

Blood Pressure: The change in the systolic blood pressure was negligible. At the same time there was a preliminary fall in the diastolic pressure of less than 10 points, which was recovered by the time the anesthesia was started. Thus there was no increase of pulse pressure during this preanesthetic interval. After anesthesia was established and the operation begun, the normal systolic pressure of 104 increased just before the middle of the operative procedure to its maximum of 136, following which there was a decline to 128 at the end of the operation—a moderate operative effect. The diastolic pressure, following the establishment of anesthesia and during the operation, tended to fall slightly from 73 to an average of 58, thus increasing the pulse pressure by 30 points, from 40, its normal, to 70, during the maximum effect of the operation. This compares with an increase of pulse pressure of 58 in the case of exophthalmic goiter under comparable conditions.

Leukocytes: There was an insignificant change in the total white cell count, namely, a fall from 5,800 to 5,650. There was a fairly definite increase in the total white cell count during the operation from 5,650 to its maximum of 12,500

at the peak of the reaction, an increase of 6,850 as compared with 10,400 in the case of exophthalmic goiter. At the end of the operation the total white cell count fell to 9,800.

Differential Blood Count: During the preoperative period, the percentage of polymorphonuclear leukocytes increased slightly. During the operation there was a relatively moderate fall from 70 per cent to the low point of 62 per cent, a fall of 8 per cent. This was entirely recovered, for at the end of the operation the percentage of polymorphonuclears was 70. These changes differ strikingly from those seen under comparable conditions in the patient with exophthalmic goiter. During the preoperative waiting period there was really no change of significance in the percentage of mononuclear cells, which had fallen from 30 to 25. During the operation there was a slight rise of the mononuclears from 25 to 38 per cent, a rise of 13 per cent; a fall to 30 per cent occurred at the end of the operation, thus making a moderate change in the mononuclear count.

Blood Sugar Determinations: The blood sugar was not studied in this case.

Rectal Temperature: There was a slight rise of rectal temperature from 98.8 F. before operation to 99.2 F. at the height of operation and 99 F. at the end of the operation. There was an increase of rectal temperature of 0.4 F. as compared with 2.4 F. in the patient with exophthalmic goiter.

Postoperative Period of Subsidence of Clinical Reactions.—Following the completion of the operation, there was a fairly prompt recovery, particularly on the part of the pulse rate and blood pressure.

Pulse: The pulse rate was rapidly restored to normal within an hour following the close of the operation, following which there was a slight fall, and at the end of the day the pulse rate was 84.

Blood Pressure: Similarly, the systolic blood pressure recovered its normal level within an hour, namely, 108, which was maintained to the end of the day. The level of diastolic pressure returned to normal at the end of the operation and remained so to the end of the day.

Leukocytes: A progressive increase in the leukocyte count during the postoperative period was found. As previously stated, we feel that this increasing leukocytosis was due largely to the reaction to the wound and was not a response to the operative procedure per se. Thus, a rise in the total white cell count was noted from 9,800 at the end of the operation to 23,900 at the end of the day, seven and one-half hours later. During this same interval the percentage of polymorphonuclear leukocytes had risen from 70 to 96 at the end of the day, and the percentage of mononuclears had fallen from 30 to 4. This reaction is rather strikingly similar to the late leukocytic reaction in the case of exophthalmic goiter, which is another reason for believing that the reaction to the wound and not the suprarenal factor is the cause in both cases, since in other respects there were such remarkable differences.

Rectal Temperature: There was no change in the rectal temperature.

In summarizing, there were only moderate subjective and objective clinical reactions in this patient with mildly toxic adenoma during the period of anticipation of the operation, during the immediate preanesthetic period and during the operation. The responses described were all mild or moderate and are to be contrasted with the definitely marked reactions which we found during operation on the patient with exophthalmic goiter. The operative reactions in the patients with exophthalmic goiter and adenomatous goiter are strikingly proportionate to the degree of toxicity indicated clinically and in the metabolic rate. The difference is entirely one of degree, the pattern and tendency of each factor of reaction being the same.

Clinical Response to the Injection of Epinephrine Hydrochloride.—The reactions to the subcutaneous injection of 0.5 cc. of 1:1,000 solution of epinephrine given on April 4, 1933, one day before the operation for excision of the adenoma, were the same as those noted during operation and previously described in case 1. Thus, the immediate preinjection status was one of quiet and composure, and there were no changes noted in any of the possible clinical responses.

Pulse: The preinjection pulse rate averaged 98. Following the injection of epinephrine hydrochloride, the pulse rate rose promptly and abruptly, but moderately, from 100 to 116; it returned promptly to the preinjection level, and

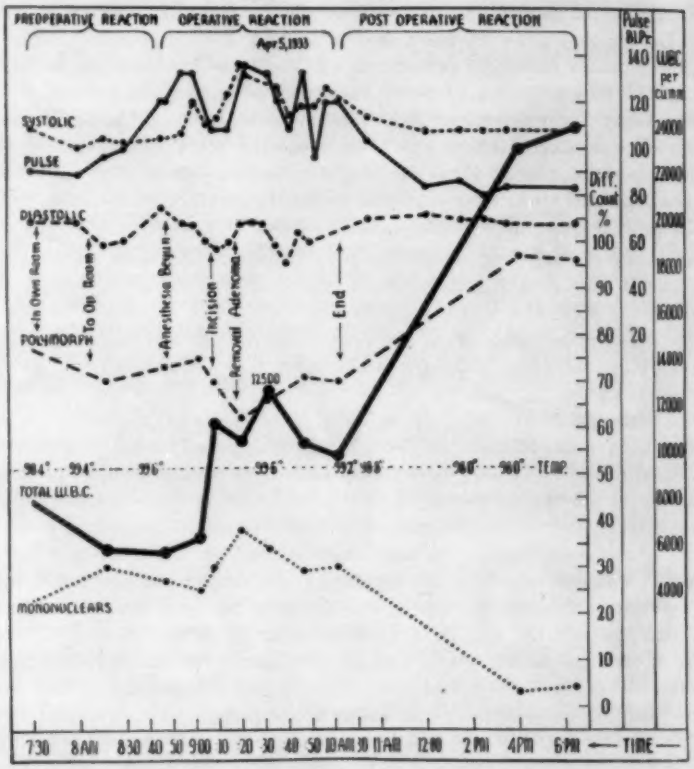

Chart 3 (case 2).—Clinical chart in a case in which a mildly toxic adenoma was excised. The basal metabolic rate after the preparatory treatment with iodine was plus 5.9 per cent. The chart is divided into the preoperative, operative and postoperative periods and shows graphically the relatively mild responses which are produced in the pulse, blood pressure, leukocytes, blood sugar and temperature in consequence of the operative procedure.

then remained at an even level of 104 throughout the period of observation, which was from 11:00 a. m. to 12:30 p. m. There was thus a slight early increase in the pulse rate which soon returned to normal.

Blood Pressure: The systolic normal pressure was 110. Following the injection of epinephrine hydrochloride there was a temporary fall to 84 with a sub-

sequent abrupt vertical rise to 126, following which there was a gradual fall to 100 at the end of the period of observation. The diastolic pressure began with a normal of 72, ran parallel with the systolic pressure, fell temporarily to 50 and then promptly returned to 68, thus increasing the normal pulse pressure 18 points, from 40 to 58. Following this the diastolic pressure fell but soon recovered and remained constant at a level averaging 66 to the end of the period of observation. There was thus a moderate increase of 18 in the pulse pressure at the height of the reaction to the epinephrine hydrochloride. This is to be

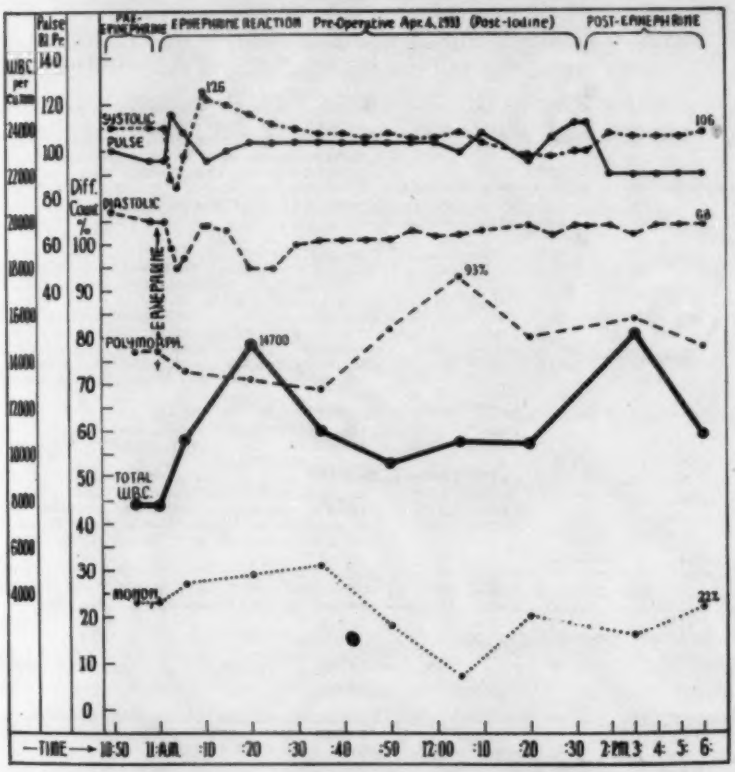

Chart 4 (case 2).—Clinical chart showing the changes which occur in the pulse rate, blood pressure, leukocytes, blood sugar and temperature in response to the subcutaneous injection of 0.5 cc. of 1:1,000 solution of epinephrine. The observations were made on the day before operation. A comparison of charts 3 and 4 shows a marked similarity in the clinical reactions produced by operation and by the epinephrine hydrochloride. The degree of response is approximately the same in each case. Both charts are to be compared with the observations in charts 1 and 2 under comparable conditions in the case of toxic exophthalmic goiter.

compared with an increase of 29 points of pulse pressure under comparable circumstances in the case of exophthalmic goiter.

Leukocytes: The total white cell count rose from the preinjection level of 7,850 to 14,700 twenty minutes after the injection; it fell in the middle of

the test and remained at a constant level, averaging about 10,500. There was a rise in the percentage of polymorphonuclear leukocytes from the preinjection normal of 77 to 93, an increase of 16 per cent at the end of an hour following

TABLE 2.—*Clinical Reactions to the Hypodermic Injection of Epinephrine Hydrochloride in Case 2*

Time	Pulse	Respiration	Blood Pressure	Blood Count	Comment
10:50	100	15	110/74	W.B.C. 7,850 Pmn. 77% Mono. 23%	Calm and relaxed; fine tremor of hands; hands dry; mild pulsations in neck
10:58	96	16	110/70	.....	Status unchanged
11:01	...	..	.....	.....	Injection of epinephrine hydrochloride (0.5 cc. of 1:1,000 solution)
11:02	96	..	110/70	.....	Status unchanged
11:03	116	18	88/58	.....	Increased depth of respiration together with increased rate; deep sigh; feeling of fainting
11:04	...	18	84/50	.....	Circumoral pallor marked; increased neck and cardiac pulsations; slightly increased hand and finger tremor; hands moist; "feet cold"
11:06	108	20	98/54	W.B.C. 10,600 Pmn. 73% Mono. 27%	"Pounding of heart;" increased throbbing of neck; pallor of fingers
11:10	...	..	126/68		
11:11	96	22	122/68	.....	Status unchanged
11:15	100	20	120/66	.....	Respiration deeper; cardiac and neck pulsations still marked; hands mildly moist; tremor of fingers still present
11:20	104	16	116/50	W.B.C. 14,700 Pmn. 71% Mono. 29%	Neck and cardiac pulsations moderately marked; "feet feel as thought they were getting warmer;" actually cold to the palpating hand
11:25	104	14	112/50	.....	Circumoral pallor less; hands slightly warmer, are mildly moist; finger tremor still present
11:30	104	14	110/60		
11:35	104	18	108/62	W.B.C. 11,000 Pmn. 69% Mono. 31%	Status the same; cardiac and neck pulsations still moderately marked; feet still cold; hands still moist; tremor still exaggerated
11:40	104	14	106/62		
11:45	104	18	106/62	.....	Feet still cold; status about the same otherwise; cardiac pulsations distinctly less; feels quite relaxed and similar to status prior to injection of epinephrine hydrochloride; finger tremor very mild although definite; hands mildly moist
11:50	104	16	108/62	W.B.C. 9,600 Pmn. 82% Mono. 18%	
11:55	104	16	106/66		
12:00	104	16	106/64	.....	Status the same
12:05	100	16	108/64	W.B.C. 10,500 Pmn. 93% Mono. 7%	Status the same; blood flows freely from stylet wound in blood puncture
12:10	108	14	104/66		
12:20	96	24	98/68	W.B.C. 10,400 Pmn. 80% Mono. 20%	Status essentially the same; hands quite warm, mildly moist; relaxed generally; feet feel warm objectively and subjectively
12:25	106	17	96/64		
12:30	112	18	100/68	.....	Patient quite relaxed; hands and feet quite warm; mildly moist; neck and cardiac pulsations now back to normal
12:35	112	18	100/68		
12:45	...	..	.....	.....	Dinner (end of reaction)
2:00 p.m.	90	16	108/68		
3:00	90	18	106/64	W.B.C. 15,100 Pmn. 84% Mono. 16%	
4:00	90	18	106/68		
5:00	90	18	108/68		
6.00	90	18	108/68	W.B.C. 10,850 Pmn. 78% Mono. 22%	

the injection. Then there was a moderate fall to 82 per cent at the end of the period. The mononuclear leukocytes rose slightly from the preinjection normal of 23 per cent to 29 per cent during the early period of observation, fell to a low of 7 per cent and recovered to 16 per cent at the end of the period of observation.

Postepinephrine Injection Period.—All the factors of response were observed from the end of the period of observation at 12:30 p. m. to 6:00 p. m. It is

unnecessary to elaborate in the case of each, and it may be briefly stated that there were no significant changes in any of the factors of response during this period except a temporary increase in the total white cell count at 3:00 p. m. In other words, the reactions had practically subsided in a period of one and one-half hours after the injection of epinephrine hydrochloride.

Comment.—The clinical reactions produced by excision of a mildly toxic adenoma in a woman, 29 years of age, tended to be of the same general character, but were relatively far milder (chart 3) as compared with the sharp reactions in the case of the patient with exophthalmic goiter (chart 1). It is unnecessary to enumerate them in detail. On the day before operation, an epinephrine test was done (table 2), and by comparison with chart 4, it is seen that the clinical reactions to the subcutaneous injection of 0.5 cc. of epinephrine hydrochloride were

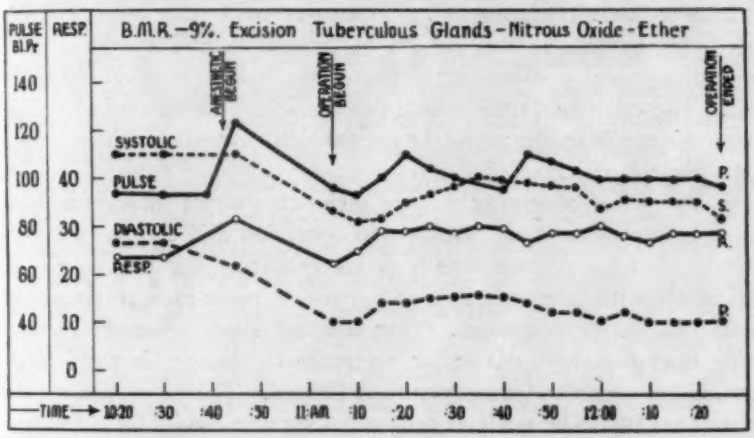

Chart 5 (case 3).—Clinical chart of a control patient showing the absence of clinical reactions on the part of the pulse rate, blood pressure and respirations during excision of tuberculous glands of the neck. The chart shows the absence of clinical response to anesthesia and operation in the patient without hyperthyroidism.

also relatively mild and of the same character as those provoked by operation. Furthermore, it is noted, particularly with reference to charts 1 and 2, that the reactions to operation and to epinephrine were approximately equal and proportional to the degree of toxicity manifested by the patient, clinically and by the metabolic rate. The responses to the injection of epinephrine hydrochloride in the patient with adenoma (chart 4) were far less acute than the reactions in the patient with exophthalmic goiter, observed under similar conditions.

CASE 3.—*Operative Response on the Part of Systolic and Diastolic Blood Pressure, Pulse Rate and Respiration in a Control Case.*

In order to test the factors of anesthesia and operation in other than patients with hyperthyroidism, a number of control subjects were studied with reference

to the reactions of the blood pressure, pulse rate and respiration. The same type of anesthetic was given, and an operation was chosen of a nature somewhat similar to thyroidectomy, namely, excision of tuberculous glands of the neck. The subject chosen for this report was a woman, aged 25, who was in general good health, excepting for the tuberculous glands, and had a basal metabolic rate of minus 9 per cent before operation. There were no significant reactions to the anesthetic or to the operative procedure (chart 4). There was a mild rise in the pulse rate when the anesthetic was started. This returned to normal at the beginning of the operation and remained practically so throughout the operation. There was no rise of the systolic pressure or significant fall of diastolic pressure at the beginning of the anesthesia. In fact, at the time the operation was begun, both fell moderately and then remained at a fairly constant level throughout the operation. Similarly there was no change of significance in the respiratory rate.

COMMENT

In a nonsensitive patient, as compared with the sensitive patient with hyperthyroidism, the factors of anesthesia and operation do not have an appreciable effect on the pulse rate, blood pressure and respirations. The etiologic factor which produces such sharp clinical reactions during operation in the sensitive patient with hyperthyroidism is absent in the control patients.

Finally, after observing a large series of control subjects with particular reference to their reactions to operation and to epinephrine, we can state that the responses to both are relatively negative. This holds particularly with reference to blood pressure, pulse rate, respiration and general subjective responses. Our detailed study of control subjects during operation with particular reference to changes in the leukocyte count, blood sugar and temperature is limited. Therefore, general comparisons are not to be made at present. Our purpose is, for the moment, to explain simply the reactions which were found in the active cases of hyperthyroidism. Further studies are being made on normal subjects.

SUMMARY

Observations have been made on the clinical reactions exhibited by patients subjected to thyroidectomy. These reactions are seen in a mild degree during the period of anticipation of operation and more intensely during the course of operation.

Preoperative Period.—As a result of our studies thus far, we believe that the reactions of the sensitive, toxic patient with hyperthyroidism to operative procedures such as thyroidectomy are definite and readily recognized. The element of emotion, apprehension and fear, with its stimulating effect on suprarenal activity, has been mentioned. The psychic emotional effect of the anesthesia, the element of starvation, operative trauma, possible hemorrhage and other factors produce a definite series of events. These are a preoperative increase of pulse

rate and of systolic blood pressure, and fall of the diastolic pressure. There is also some increase of blood sugar and temperature.

Operative Period.—Immediately following the beginning of the anesthesia and during the first twenty-five to thirty-five minutes, the operative reactions reach a maximum characterized by a rather sharp rise of the systolic pressure with a fall of the diastolic pressure. Thus, the blood pressure and hence the load on the heart are definitely increased. Thereafter, there is a gradual subsidence of the systolic pressure and a rise in the diastolic pressure with a restoration at the end of operation of the pulse pressure to the preoperative level. There is a synchronous increase on the part of the pulse, which rises sharply during the early part of the operation and usually falls toward the end. The total white cell count increases soon after the incision is made and continues to rise during the operation and the postoperative period. There is a characteristic behavior of the leukocytes, as shown by the differential count in which, during operation, there is a striking mononucleosis characterized by a sharp increase in the percentage of mononuclear cells. Simultaneously there occurs a marked decrease in the percentage of polymorphonuclear cells. Following the peak of the operative reaction, there is a striking reversal of the picture. The mononuclears fall to a point well below the preoperative level. A continued decline in the mononuclears and an increasing rise in the polymorphonuclears occur during the postoperative period. The blood sugar increases just before and during the operation. We also find an elevation of the rectal temperature which, together with the increase in blood sugar, is sustained and persists for a time during the postoperative period. These reactions briefly described as occurring during operation are reproduced in a remarkably parallel manner before operation by the hypodermic administration of epinephrine hydrochloride. A remarkable similarity is noticed in comparing the behavior of all the reactions manifested during the operation with those that can be produced by the administration of epinephrine hydrochloride. The differences are largely of degree and not of general character. So striking is this parallelism that it has seemed to us warranted to believe that the characteristic clinical reactions which are produced by thyroidectomy for hyperthyroidism are caused by hypersecretion of epinephrine resulting from stimulation of the suprarenal glands. This hyperactivity of the suprarenals is secondary to the disturbing effect of emotion, apprehension, pain, conscious or subconscious manipulation, anesthesia, trauma and all the other factors that comprise a major surgical procedure.

We are not at this time considering the means of obviating these distressing and at times dangerous operative reactions. Crile has pointed the way in the development of his method of anoci-association. Further studies will doubtless lead to the discovery of chemical, physiologic or

surgical means for completely neutralizing or at least greatly minimizing the effect of suprarenal activity during operative procedures. Thyroidectomy in the case of the highly toxic patient suffering with hyperthyroidism would then be less of an ordeal and the postoperative period would be comfortable and even safer than it is at the present time.

CONCLUSIONS

Critical studies of the clinical responses of patients with hyperthyroidism during the operation of thyroidectomy indicate that a number of characteristic reactions are provoked by such operative procedure.

The operative reactions observed in the patient with hyperthyroidism have been approximately duplicated in character and degree by a small dose of epinephrine hydrochloride subcutaneously administered to the same patient several days before operation.

The similarity of the operative reactions and the responses to the hypodermic injection of epinephrine hydrochloride in the same patient indicate that the former are the result of increased amounts of epinephrine liberated from the suprarenal glands which have been abnormally activated by the various factors comprising the operation.

The manifestations of suprarenal activity which are observed in the clinical reactions before and during thyroidectomy for hyperthyroidism include tremor, throbbing, flushing, perspiration and sharp increases in both the systolic blood pressure and the pulse pressure. There are also a marked increase in pulse rate, an increase in blood sugar and an elevation of body temperature. Furthermore, there are a striking leukocytosis and a marked change in the differential count. There is a definite mononucleosis which begins just before the administration of the anesthetic and continues to increase to a maximum reached in from thirty-five to forty minutes. Synchronous with this absolute and relative increase in the mononuclear cells, there is a sharp fall in the percentage of polymorphonuclear cells. After these maximal changes during operation, the picture is reversed; a sharp fall in the percentage of mononuclear cells occurs with an abrupt rise in the percentage of polymorphonuclear cells to the end of the operation and even beyond. All the operative reactions in the patient with hyperthyroidism were similarly brought out by the administration of epinephrine hydrochloride to the same patient several days previous to operation.

It would appear accordingly that as a result of thyroidectomy for the relief of hyperthyroidism, there is a liberation of an excessive amount of suprarenal secretion. The operative reactions are thus caused by the stimulating effect of this increased amount of epinephrine on the sympathetic nervous system, which has been rendered hypersensitive by the existing hyperthyroidism.

FIFTY-FOURTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY

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TUBERCULOSIS

Human and Bovine Infection; Extrapulmonary Tuberculosis.—Chang [1] analyzed 200 cases of extrapulmonary tuberculosis to determine the percentage of human and bovine infections. In the whole group, 72.5 per cent were infected with tubercle bacilli of the human type and 27.5 per cent with the bovine type of organism. However, in young children the infection was predominantly bovine (71 per cent in the age group from 1 to 5). This indicates that milk-borne infection still plays a prominent rôle in the younger groups and that pasteurization of milk and tuberculin testing of cattle are still not universal.

Diagnosis of Surgical Tuberculosis.—Blair and Hallman [2] advocated attempting to culture the tubercle bacillus as an aid in establishing definite diagnoses. One hundred and fifty specimens of synovial fluid, urine, pus, tissue and pleural exudate were studied. One hundred and six of the specimens were nontuberculous in origin and 44 were tuberculous. The method of culture was that used by Cooper and Uyei. The culture medium was made of crystal violet, glycerin water and

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This report of progress is compiled from a review of 176 articles selected from 293 titles appearing in medical publications approximately between Nov. 4, 1933, and March 1, 1934. Only those which seemed to represent progress were selected for review.

1. Chang, C. S.: New England J. Med. **209**:690, 1933.

2. Blair, J. E., and Hallman, F. A.: Diagnosis of Surgical Tuberculosis: Comparison of Diagnosis by Inoculation of Guinea-Pigs and by Culture, Arch. Surg. **27**:178 (July) 1933.

potato. Microscopic tests showed tubercle bacilli in smears in from two to four weeks. A culture was usually positive before the time required for the guinea-pig test had elapsed.

Heliotherapy and Orthopedic Treatment in Surgical Tuberculosis.—Rollier [3] presented a plea for the treatment of tuberculosis of the joints along conservative lines. He dealt specifically with the disease of the various joints and described briefly the type of treatment employed for each in his clinic. He would rely on the sun and carefully applied physical therapy to develop muscular support to the part, to reform the joint and to restore, at least to some extent, the motion of the joint. He regarded the cold abscess as a "small laboratory where the immunizing bodies were developed." He would aspirate such an abscess only in an attempt to prevent rupture. He would, however, resort to operation to secure good drainage of secondarily infected sinuses with the hope of preventing amyloid disease.

PYOGENIC INFECTIONS

Suppurative Tenosynovitis of the Hand.—In a report on 200 cases of suppurative tenosynovitis of the hand from Payr's clinic in Leipzig seen between 1919 and 1932, Deicke [4] stated that most of the cases followed insignificant injuries. Cultures were taken only in the more severe cases. Of these, 72 per cent showed streptococci and 28 per cent staphylococci. The thumb and middle finger were affected in 57 per cent of the cases. Increased frequency of the lesions during summer and autumn was observed by the author. The thenar space was involved 19 times and the midpalmar space 35 times. In 61 cases, extension to the forearm occurred. In 1 of these, osteomyelitis of the radius developed. In 52 cases sloughing of the tendon occurred. With the appearance of spindle-shaped swellings of the fingers in neglected cases, involvement of the bone (16 cases) and joint (6 cases) was suspected. In 4 cases, both the bone and the joint were diseased. The wrist was involved 4 times. One patient died, and 2 patients were subjected to amputation. Ankylosis of the wrist occurred in 1 case. The author recommended early small incisions and the induction of Bier's passive hyperemia. Early motion was stressed. The results in terms of function in cases of synovitis were good in 46.5 per cent, fair in 23.9 per cent and bad in 29.6 per cent. In 129, phlegmon results were good in 30.5 per cent, fair in 17 per cent and bad in 35 per cent; the mortality rate was 8 per cent. The age of the patient influenced the results obtained, the poorest results being obtained in the aged.

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3. Rollier, A.: Surg., Gynec. & Obst. **37**:220, 1933.
4. Deicke, H.: Beitr. z. klin. Chir. **158**:461, 1933.

Nontuberculous Abscess of the Psoas Muscle in Childhood.—Five cases of presumable primary infections of the psoas muscle were described by Klages.[5] A limp, pain in the leg, inguinal adenopathy, increased lumbar lordosis and fever all pointed to the site of the lesion. The outlines of the psoas muscle might be changed in the roentgenogram. Following aspiration of pus, drainage by the extraperitoneal route was advised.

ARTHRITIS

Rheumatism; Clinical Experimental Investigation.—Copeman[6] considered the facts that the National Health Insurance had to pay nearly 20,000,000 pounds per annum to sufferers from industrial rheumatism and that 6,000,000 weeks of work were lost annually on account of the same condition were ample justification for a strenuous national campaign against the "captain of crippledom." He outlined a comprehensive scheme, and, in vindication of an active instead of a "defeatist's" attitude toward the diseases, cited the figures of the Petro Place Clinic for Rheumatism, which showed 18.6 per cent cures and 54.8 per cent improvements after treatment.

Development of Neuro-Arthropathies.—Alajouanine and Mauric[7] called attention to the fact that close observation, clinical and roentgenologic, of patients with neurologic diseases (particularly tabes and syringomyelia) revealed not only little known aspects of the arthropathies but also a recognizable prearthropathic state. The latter consisted of localized bony overgrowth simulating hypertrophic arthritis or a definite atrophy of the substance of the bones. The tarsal joints, fingers and great toes were the most common sites for these seldom recognized arthropathies. Clinically, they were accompanied by what the authors called a pseudo-infectious condition. The tissues were swollen, hot and cyanotic, with dilated veins suggesting a deep sepsis. No treatment was suggested, except that 1 case was reported in which arthropathy of the midtarsal joints was remarkably improved by periarterial sympathectomy.

Sacro-Iliac Arthritis.—Willis[8] studied a large number (1,559) of human skeletons, 96 of which showed bony ankylosis in one or both sacro-iliac joints. He felt that these were brought about by one of two ways: by smooth calcification of the anterior common ligament or by irregular lipping of the periphery of the joint. Of specimens of the first type, there were 19, with an average age of 45.9 years; of the latter, there were 6, with an average age of 67 years. In 67 specimens, the

5. Klages, F.: Beitr. z. klin. Chir. **158**:171, 1933.
6. Copeman, W. S. C.: J. State Med. **41**:476, 1933.
7. Alajouanine, T., and Mauric, G.: Presse méd. **41**:1537, 1933.
8. Willis, T. A.: Surg., Gynec. & Obst. **57**:147, 1933.

average age of which was 57.3 years, there was a combination of the two types. Four pelves showed congenital obliteration of the joint. "The bone and joint changes were in direct ratio to the mechanical stress of the upright position." In persons more than 40 years of age, lipping of the axial skeleton and acetabulum was practically universal, and increased with age.

NEOPLASMS

Radiosensitivity of Tumors.—Space does not permit complete reprinting of this editorial [9] as a whole. It presented an excellent summary of the present knowledge on the radiosensitivity of tumors, however, and should be read in its entirety. Some points that were brought out were: 1. Radiosensibility of tumors is no accidental attribute but an expression of all structures as well as parent tissue. 2. Location of a tumor, particularly in bone or fat, renders it radioresistant. 3. Tumors develop resistance to both roentgen rays and radium. 4. The degree of malignancy has little to do with radiosensibility. Differences in reaction become clear when it is remembered that there are similar differences in normal cells. Sensitivity seems related to the natural life cycle of the cell. Finally, the standardization of dosage and the artificial increase in radiosensibility are reviewed.

Results of Irradiation in Treatment of Operable Osteogenic Sarcoma of Long Bones.—The controversy over the method of treatment of osteogenic sarcoma without demonstrable metastasis has long raged. Coley,[10] after a review of his own cases as well as those in the Registry of Bone Tumors, concluded that there was a growing number and an increasing percentage of five year cures in spite of pessimistic reports to the contrary. He reported 33 five year cures. The treatment of choice was amputation without biopsy or preoperative irradiation. Postoperative irradiation also probably was useless, but the use of erysipelas and prodigiosus toxins (Coley's) postoperatively was beneficial. Endothelial myeloma (Ewing's tumor) responded best to irradiation and the toxins used simultaneously.

SPINE

Ghormley [11] stated that many cases of pain low in the back were due to pathologic changes in the articular facets. These changes could often be shown roentgenographically by oblique lateral views of the spine. Treatment of pain of this type should be essentially conservative, but nevertheless there were certain indications for operation. Ghormley

9. Radiosensitivity of Tumors, editorial, J. A. M. A. **102**:619 (Feb. 24) 1934.

10. Coley, W. B.: Radiology **21**:318, 1933.

11. Ghormley, R. K.: Low Back Pain, with Special Reference to Articular Facets, with Presentation of Operative Procedures, J. A. M. A. **101**:1773 (Dec. 2) 1933.

enumerated the conditions, some or all of which should be satisfied before operation was recommended: (1) persistent or recurrent attacks of pain over a period of months, (2) pain localized to a definite area, (3) narrowing of the intervertebral disk, (4) changes in the intervertebral articulations and (5) examination of the central nervous system with negative results. It was not possible to select those patients whose trouble lay solely in the facet; therefore a lumbosacral fusion or excision of the lumbosacral articular facets was performed.

Enlargement of Intervertebral Disk Associated with Decalcification of the Vertebral Body.—Moffat [12] suggested that the enlargement of the vertebral disk seen frequently with pathologic fractures was due to simple hypertrophy of the disk and not to rupture of the nucleus. Five cases were reported to substantiate his claim.

SCOLIOSIS

Removal of Vertebral Bodies in the Treatment of Scoliosis.—Von Lackum and Smith [13] removed a vertebral body in each of 10 cases to correct scoliosis. In 5, the scoliosis was caused by a hemivertebra; in 5 others, the cause of the scoliosis was unknown. They found that removal of a dorsal vertebra was not practical because of hemorrhage and shock. The lumbar vertebrae were removed in two stages, the technic of which was described. The age of the patients varied from 1½ to 22 years, the average being 11½ years. The authors felt, however, that the operation should not be done on a person less than 6 years of age. Removal of the vertebra was in each case followed by spinal fusion and correction of the curve by means of plaster of paris jackets.

CIRCULATORY DISTURBANCES OF THE EXTREMITY

Thrombo-Angiitis Obliterans.—Samuels [14] discussed the general treatment of this disease based on experience with about 300 cases. Twelve cases were reported in detail. He stated that except in rare instances (less than 1 per cent) amputation was not indicated. Treatment consisted of: (1) rest in bed with the limb constantly horizontal, (2) prohibition of tobacco, (3) intravenous injections of hypertonic saline solution (from 2 to 5 per cent) in doses of 300 cc. every other day, depending on the severity of the case, and (4) surgical cleanliness of the affected areas with the application of anesthetic oint-

12. Moffat, B. W.: J. Bone & Joint Surg. **15**:705, 1933.

13. von Lackum, H. L., and Smith, A. De F.: Surg., Gynec. & Obst. **57**:250, 1933.

14. Samuels, S. S.: Gangrene Due to Thrombo-Angiitis Obliterans: Further Experiences with Treatment, J. A. M. A. **102**:436 (Feb. 10) 1934.

ments in the painful stage. Samuels believed that sympathectomy and ganglionectomy had no place in the treatment of this condition.

[Ed. Note.—There is much still to be learned concerning the peripheral circulatory disorders. This report, if confirmed by others, would suggest that less radical therapy was indicated.]

Topical Diagnosis of Embolism of the Extremities.—Paresthesia, pain, coldness, pallor and anesthesia for small movements and muscular palsies were the usual signs, according to Dick,[15] of local ischemia, but these signs did not permit the localization of an embolus in the extremity because of the development of collateral circulation. Occasionally local pain might be felt on the lodgment of an embolus. Rarely was the embolus palpable, even in emaciated persons. Local tenderness at the site of lodgment of the embolus as well as absence of pulsation was sometimes of help. Arteriography was of value in localizing the embolus in 1 case. The poor results in attempted embolectomy were usually referable to: (1) repeated showers of emboli occurring in severe cardiac or vascular disease, (2) an embolus that was allowed to remain in place so long that thrombi extended from it into the smaller vessels owing to injury of the vascular intima and (3) often difficult localization of the point of vascular occlusion.

INTERNAL DERANGEMENT OF THE KNEE JOINT

Osteochondritis Dissecans.—After describing some cases of osteochondritis dissecans, especially those in which the knee joint was affected, Fairbank[16] discussed the various theories of causation which have been advanced to explain this condition. He came to the conclusion that trauma alone could explain all cases satisfactorily. The mechanism of the trauma, in the case of the knee joint, was taken to be a violent rotation inward of the tibia which drove the tibial spine against the inner condyle of the femur.

[Ed. Note.—The editors believe that the etiology of osteochondritis dissecans is more complex than this article would lead one to believe. There is equally good evidence for an embolic theory of causation.]

Diagnosis and Results of Injuries of the Meniscus.—In 134 arthrotomies performed at Schloffer's clinic at Praha, Spira[17] found 84 injuries of the menisci. Most of the cases were traumatic in origin. The meniscal lesions observed at operation were: tear of the anterior horn, 11 times; tear of the posterior horn, 9 times; longitudinal tear, 6 times; "bucket handle" tear, 14 times; transverse tear, 15 times;

15. Dick, W.: Beitr. z. klin. Chir. **158**:481, 1933.
16. Fairbank, H. A. T.: Brit. J. Surg. **21**:67, 1933.
17. Spira, E.: Beitr. z. klin. Chir. **158**:1517, 1933.

displacement of the anterior horn, 14 times, and indefinite displacement, 4 times. In the patients reexamined (postoperative period not given), an excellent result was observed in 72.1 per cent, a good result in 22.4 per cent and a poor result in 6.6 per cent.

THE FOOT

Manipulative Treatment of Painful Feet.—That manipulative treatment, followed by exercises to maintain and improve the flexibility and strength of the feet, brought about a cure in 83 per cent of cases of "chronic foot strain" was stated by Wiles.[18] The joints most commonly affected in the first instance were the midtarsal joints, but in late cases it was sometimes impossible to find the primary site of strain and formation of adhesions. Certain cases of chronic arthritis were suitable for manipulative treatment, but considerable care had to be exercised in selection. The manipulative technic advocated was described.

[ED. NOTE.—Forceful manipulations for disabilities of the foot, an extremely popular procedure by certain cultists and physicians, is fraught with considerable dangear unless careful selection of cases is made. The cases which respond most favorably to this procedure are rigid flatfoot without too great bony distortion and early arthritic deformities when extensive ankylosis has not occurred. Manipulation must be followed in every case by apparatus to maintain temporarily the corrected position and by prolonged exercise to regain strength. In the feet in which marked bony deformation has occurred, plastic operations on the bone should be the therapy of choice.]

MISCELLANEOUS

Arthropneumoroentgenography.—In a well illustrated article, Oberholzer[19] described his experience with visualization of joints. In his hands diagnosis of most internal derangements could often be made accurately by this method.

Serum Treatment of Gas Edema.—Löhr[20] believed that there was evidence of definite clinical value of the German serums used in the prevention and treatment of gas gangrene. He felt that a multivalent serum should be used since of the many strains of Bacillus welchii known all were pathogenic. The immediate intramuscular injection of serum in large amounts was advocated since the spread of the infection was a matter of hours.

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18. Wiles, P.: Brit. M. J. **2**:563, 1933.
19. Oberholzer, J.: Beitr. z. klin. Chir. **158**:113, 1933.
20. Löhr, W.: Beitr. z. klin. Chir. **158**:571, 1933.

Rupture of the Quadriceps Tendon.—Lenormant and Olivier [21] found rupture of the quadriceps tendon to be comparatively rare. The mechanism of such injury was a severe muscular effort to regain the upright position when the knee was suddenly flexed. The patient might fall onto the knees, but the rupture was due to the pull of the muscle and not to a direct blow. Certain predisposing causes were found which accounted for the frequency with which the lesion was bilateral. Rupture occurred in patients over 40 years old. Diabetes, chronic arthritis and arteriosclerosis were possible factors. It was seen associated with calcified deposits in the quadriceps tendon. Treatment consisted of operative repair with catgut or fascia and early mobilization. Age was no contraindication to operation as repair could be done under local anesthesia. The results were uniformly good. An interesting comparison was made with the results in a series of 85 cases in which no operative treatment was used. These results were: good, 34; poor, 35, and bad, 16.

ORTHOPEDIC OPERATIONS

Hip Fusion Operation.—Chandler [22] described an operation using a massive graft from the trochanter and upper end of the femur, similar to that of Hibbs. The approach was by a long vertical-lateral incision through the gluteus medius, tensor fascia lata and vastus lateralis. Heavy osteoperiosteal flaps of cancellous and cortical bone were reflected from the anterolateral and posterolateral aspects of the trochanter. A long massive graft, including the great trochanter, the distal lateral aspect of the neck and the upper end of the femur, was cut out and turned end for end. The upper end of the graft was inserted into a recess in the ilium made by elevating a flap of the outer table. The distal end of the graft lay in the groove from which it was removed and was covered by the osteoperiosteal flaps which fell back over it.

Extra-Articular Bone Graft Treatment for Tuberculosis of the Hip Joint with Especial Study of Primary Failures of Fusion.—Haas [23] studied the results in 50 cases of extra-articular fusion of the hip for tuberculosis in children. The average age was 7 years. Six patients presented sinuses at the time of operation, but only 1 failed to heal during convalescence. The average duration of the disease was 4.3 years. Forty per cent, or 20 patients, required more than one operation. Conditions which favored fusion were: (1) chronicity and quiescence of the disease, (2) approximation of the trochanter to the acetabulum, (3) little motion in the hip and (4) absence of abscess or sinus at the time of operation, although the presence of these did

21. Lenormant, C., and Olivier, C.: Presse méd. **41**:1561, 1933.
22. Chandler, F. A.: J. Bone & Joint Surg. **15**:947, 1933.
23. Haas, S. L.: J. Bone & Joint Surg. **15**:743, 1933.

not necessarily mean disaster. The routine operation was to turn flaps of bone down from the ilium to between the trochanter and femur, unless failure of fusion was anticipated, in which event an osteoperiosteal graft was also taken from the tibia.

Extra-Articular Arthrodesis of the Shoulder.—Watson [24] concluded that a solidly arthrodesed joint was the best end-result to be obtained in tuberculosis of the shoulder joint. He believed that the extra-articular method was best in these cases and devised a new operation which had yielded excellent results in the 3 cases he reported. Through a straight incision over the joint of the shoulder the deltoid muscle was removed subperiosteally from its entire origin and turned downward. The cortical layer of bone was removed from the whole acromion process. Without opening the capsule, a bone flap including the greater tuberosity was levered out without breaking it from the humerus. Partial osteotomy of the clavicle was then performed under its outer end, and the spine of the scapula was also partially fractured at a similar level. This allowed the acromion to be depressed far enough so that it was securely wedged beneath the flap of bone raised from the humerus on abduction. The wound was closed in layers and the arm immobilized in a plaster spica.

A New Method of Arthrodesis of the Shoulder Joint.—Brett [25] pointed out that though bony union resulted, in many cases the result in fusion of the shoulder joint was unsatisfactory because of loss of the angle of abduction during the period of immobilization. He attributed this to faulty scapular fixation. He advocated, in addition to the usual arthrodesis (removal of cartilage from the glenoid and head of the humerus), apposition of the acromion to the great tuberosity and fixation of the humerus and scapula by a dowel graft driven through the head of the humerus and into the glenoid and the body of the scapula. He relied on this graft to maintain the desired abduction until union was solid. Excellent results were obtained in 2 cases.

Spinal Fusion by Simplified Technic.—Henry and Geist [26] advocated spinal fusion by "feathering" the laminae with a sharp hand chisel and gouge, thus avoiding the use of a mallet. In addition, the spinous processes were broken down, and a mass of small bone chips removed from the tibia was placed over the bony bed. Good results were obtained in 75 cases by this method.

[ED. NOTE.—This method was similar to that used at the Massachusetts General Hospital for a number of years, except that at that hospital an osteoperiosteal graft was preferred to bone chips, and the

24. Watson, J. R.: J. Bone & Joint Surg. **15**:862, 1933.
25. Brett, A. L.: J. Bone & Joint Surg. **15**:969, 1933.
26. Henry, M. O., and Geist, E. S.: J. Bone & Joint Surg. **15**:622, 1933.

mallet was used over the spine. One of the editors has avoided if possible the use of the mallet on the spine in children, thus diminishing shock.]

Operative Treatment of Sacro-Iliac Disease.—Harris [27] reported the results of sacro-iliac arthrodesis in 67 cases. The diagnosis of sacro-iliac disease was made in 296 cases, i. e., 67.5 per cent of all cases examined in which there was pain in the lower portion of the back. Operation was advised but refused in 45 cases, and was not advised in 201 of the 296 cases. The average age in the cases in which operation was performed was about 33 years. The average time of palliative treatment before operation was done was 4.6 months. The Smith-Petersen technic was used. The value of the roentgenographic diagnosis in sacro-iliac strain, except to rule out disease, was questioned. The results in the 67 cases were as follows: freedom from symptoms, 46, or 68.6 per cent; partial relief, 12, or 17.9 per cent; no relief, 2, or 3 per cent; unable to trace, 6, or 8.9 per cent, and dead, 1, or 1.5 per cent. Fusion was done in 3 cases a second time because of persistent symptoms. At operation the grafts were found solid, and though the patients got well, no cause was found for the persistent symptoms. Harris advocated fusion by the Smith-Petersen technic for tuberculosis of the sacro-iliac joint, as well as for cases of persistent strain.

Amputation Through the Lower Third of the Leg for Diabetic and Arteriosclerotic Gangrene.—Smith [28] described the technic for amputation in the lower part of the leg for arteriosclerotic and diabetic gangrene and reported illustrative cases. The stumps were drained, the drain being removed without taking down the entire dressing. Too frequent dressings were discouraged. He preferred to avoid the guillotine amputation since the stumps following this procedure were often slow in healing, frequently developed osteomyelitis in the end of the bone and at times were painful. The author would also avoid the Gritti-Stokes operation, trying as often as possible to preserve the knee joint.

Recurrent Dislocation of the Patella.—Cole and Williamson [29] listed the predisposing factors in recurrent dislocations of the patella as follows: (1) genu valgum, (2) underdevelopment of the lateral femoral condyle, (3) relaxation of the medial capsule and other patellar attachments and (4) abnormal lateral displacement of the tibial tubercle. Operative procedures were divided into three groups: (1) those directed toward tightening and reenforcing the relaxed structures on the medial

27. Harris, C. T.: J. Bone & Joint Surg. **15**:651, 1933.

28. Smith, B. C.: Amputation of Leg Through Lower Third of Leg for Diabetic and Arteriosclerotic Gangrene, Arch. Surg. **27**:267 (Aug.) 1933.

29. Cole, W. H., and Williamson, G. A.: Chronic Recurrent Dislocation of the Patella, J. A. M. A. **102**:357 (Feb. 3) 1934.

side of the patella, (2) those attempting to straighten the line of pull and (3) those that raised the lateral femoral condyle. The methods used were fascial transplants in the first group, transplantation of the tibial tubercle in the second group and raising the anterior surface of the lateral condyle in the third group.

FRACTURES

The Abduction Method, Considered as the Exponent of a Treatment for All Forms of Fracture at the Hip in Accord with Surgical Principles.—Whitman [30] discussed the methods of treating fractures of the neck of the femur, including the abduction (Whitman) method, the methods of traction and those of internal fixation. He stated that for the average patient and for the average fracture (of this type) "there can be no alternative for the abduction method," and that according to statistics union of the medial fracture was obtained in about 65 per cent of cases in which this method of treatment was used. The failures in 35 per cent were due either to defective treatment or to incapacity for repair. The former should be treated by open operation, and the latter by the reconstruction procedure.

Treatment for Fractures of the Neck of the Femur.—Leadbetter [31] advocated for fractures of the neck of the femur manual closed reduction with the patient under a general anesthesia and fixation in plaster for from ten to twelve weeks. The manipulation described by the author consisted in flexion of the thigh and knee to a right angle with traction on the femur in its long axis with the thigh slightly abducted. The leg was then internally rotated 45 degrees and then slowly circumducted into extension, abduction and internal rotation maintaining the traction during the maneuver. He felt that extreme abduction and internal rotation as recommended by Whitman gave less satisfactory apposition of the fragments than a position of slight internal rotation and abduction. If reduction was satisfactory, the leg would maintain internal rotation when supported at the heel alone. He applied a plaster spica with little padding at the pelvis and none on the leg. He stressed the general care of the patient. In 31 cases, 22 patients (70.9 per cent) obtained bony union and 9 (29 per cent) obtained fibrous union. There were 4 deaths (12.8 per cent).

[Ed. Note.—The attack on this difficult problem is unremitting. Accurate reduction and complete fixation of the fracture, with careful attention to the patient's general health, are the important factors. The manipulation advocated by this author is based on sound mechanical principles.]

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30. Whitman, R.: Am. J. Surg. **21**:335, 1933.
31. Leadbetter, G. W.: J. Bone & Joint Surg. **15**:931, 1933.

Delayed Appearance of Deformity in the Vertebral Body Fractures.—Feaster [32] discussed fractures of the vertebral bodies which were not visible in the roentgenogram at the time of injury but which became so after an undetermined interval of a few weeks. He believed the trauma, although not disturbing the homogeneity of the bone, was sufficient to disturb nutrition and to weaken the bone, and later to allow more or less collapse or "wedging." This sequence of events was common enough to make roentgenologic reexamination of the spine after an interval of from two to three weeks a routine measure in all cases in which discomfort persisted. This type of case could result from slight trauma and probably constituted so-called "Kümmell's disease."

Fractures of the Spine.—Watkins,[33] in the treatment of spinal fractures, advocated the more "physiologic" treatment which briefly consisted of immediate manual reduction followed by the application of a plaster jacket in hyperextension. The jacket was split and physical therapy started in six days. Active exercise of the erector spinae muscles was considered most important during convalescence. In eight weeks the patient was allowed up wearing a brace, and exercises were continued. It was felt that within six months normal activities could be resumed. The author did not favor operative fusion for treatment of such fractures; nor did Atsatt and Wilson who discussed the paper, and who also advocated correction of the general body mechanics with a view to eliminating permanently the element of strain as a result of the injury.

Isolated Fractures of Articular Processes of Lumbar Vertebrae.—Mitchell [34] reported 5 cases of fracture of the articular processes in the spine. All were produced by a direct blow on one side of the spine. Very clear, localized roentgenograms were necessary to demonstrate the fractures. The author felt that if symptoms persisted at the end of three or four months and if there was no roentgen evidence of union, spinal fusion and removal of the loose fragments should be done. He also felt that this injury occurred much more frequently than was evident by the routine roentgenograms of the spine and that such injury might account for many persistent backaches after injuries which were attributed to adhesions, faulty posture or even neuroses.

Application of Steel Splints to Bone.—An article by Reinhold [35] cannot be abstracted without the reproduction of diagrams and photographs. It is important, however, because it may offer a solution to the

32. Feaster, O. O.: Delayed Deformity in Vertebral Body Fractures, J. A. M. A. **102**:598 (Feb. 24) 1934.
33. Watkins, J. T.: California & West. Med. **39**:246, 1933.
34. Mitchell, C. L.: J. Bone & Joint Surg. **15**:608, 1933.
35. Reinhold, P.: J. de Chir. **42**:374, 1933.

too frequent breaking of bone plates and screws, disasters which have continued in spite of the efforts of the American College of Surgeons to standardize bone plates and screws. The fault is probably due to abnormal stress brought about by the fact that drill holes and screws are not properly centered through the holes in the bone plates. The author advised an ingenious guide which is screwed onto the bone plate. Through this guide the dull holes are bored and the screws inserted. The apparatus is simple and not cumbersome. Special screws and plates are necessary, but they are of such type that they can easily be standardized.

PATHOLOGY

Clinical Significance of Structural Transformation Zones in Bones.—Transformation zones described by Loose in pathologic bone as in rickets and osteomalacia had been found by Walter [36] in normal bone which had been exposed to repeated mechanical trauma. Particularly marked changes occurred if the stresses were bending stresses. The author suggested that the so-called sympathetic lesions of the bone were probably to be explained on the basis of mechanical stress. In his opinion, the so-called aseptic necroses also fell into this group.

Tissue in Gas Gangrene.—Suder-Plassman [37] studied the muscular lesions in a fatal case of gas gangrene. He described and showed very well in photomicrographs the edema of the perimysium and the nuclear changes with chain formation, chromatolysis and pyknosis. There was edema of the perineurium with retention of the axis-cylinders and early involvement of the motor end-plates. The capillaries showed a peculiar corkscrew-like angulation. Eventually disintegration of the muscle fibers was observed with formation of "Bowman's disks."

RESEARCH

Healing of Fractures and Bone Defects After Venous Stasis.—Experiments were performed on 24 dogs by Key and Walton [38] to determine whether venous stasis helped or hindered bony union. The ulna was chosen rather than the fibula, as the latter was small and covered with muscle attachments and therefore unsuitable. In 12 dogs the ulnae were divided with an osteotome, and the veins draining that area were ligated on one side. The veins were ligated immediately in 6 dogs and after a week's interval in the other 6 dogs. In 12 dogs 0.5 cm. of the ulna was resected, and the veins were ligated similarly to those in the first group. Ligation caused marked congestion and

36. Walter, H.: Arch. f. klin. Chir. **178**:116, 1933.

37. Suder-Plassman, P.: Beitr. z. klin. Chir. **158**:603, 1933.

38. Key, J. A., and Walton, F.: Healing of Fractures and Bone Defects After Venous Stasis, Arch. Surg. **27**:935 (Nov.) 1933.

swelling lasting for two weeks. Their results were in marked disagreement with Pearce and Morton.[39] The gross specimens, microscopic slides and roentgenograms showed no difference in healing between the ligated and the unligated sides.

Studies of Immobilization of Normal Joints.—In an effort to study the effect of immobilization on joint cartilage, Ely and Mensor[40] fixed the ankle joints of 4 dogs in plaster of paris for periods varying from one to three months. Definite degenerative changes were observed both macroscopically and microscopically, the greatest changes occurring where cartilaginous surfaces were in closest apposition. The changes noted were: (1) close approximation of the articular surfaces, (2) thinning, irregularity, fibrillation and vacuolation, (3) replacement fibrosis and (4) encroachment of areolar tissues on the articular cartilage.

Osteochondritis of the Head of the Femur.—Miltner and Hu[41] reviewed the various theories as to the etiology of osteochondritis deformans juvenilis of the head of the femur (Legg-Calvé-Perthes' disease). Of the suggested causes (infection, trauma, embolism and maldevelopment), they considered that deficiency of blood supply to the head of the femur seemed the most likely. They then attempted to produce similar pathologic changes in the femoral heads of young rabbits and dogs. Interruption of the blood supply through the capsule and periosteum of the neck of the femur caused no marked changes, but when in addition to this the ligamentum teres was ligated pathologic changes developed in the head of the femur similar to those described in human osteochondritis juvenilis.

[Ed. Note.—Again the importance of vascular changes in the production of pathologic changes in the joint is demonstrated in animals. The missing link is the proof that such vascular changes occur, and the explanation of the mechanism of their production in the typical, clinical case.]

Experimental Investigations as to the Immunobiology of Bone Marrow.—While trying to produce organotropic strains of streptococci and staphylococci in the fashion of Rosenow, Erb[42] observed that the cultures of these organisms on fresh bone marrow died after a few weeks. Even the use of boiled bone led to similar results, although not quite as striking. He therefore investigated the bactericidal properties further. Animals given injections of staphylococci grown on bone marrow lived longer than those given injections of organisms grown on

39. Pearce, H. E., and Morton, J. J.: J. Bone & Joint Surg. **13**:68, 1931.

40. Ely, L. W., and Mensor, M. C.: Surg., Gynec. & Obst. **57**:212, 1933.

41. Miltner, L. J., and Hu, C. H.: Osteochondritis of the Head of the Femur: Experimental Study, Arch. Surg. **27**:645 (Oct.) 1933.

42. Erb, K. H.: Beitr. z. klin. Chir. **158**:337, 1933.

other mediums, suggesting that bone marrow might lessen the virulence of the cocci. Injury of the bone marrow by roentgen treatment resulted in marrow which lost the power of decreasing the virulence of staphylococci. The author believed that he had demonstrated bactericidal power of rabbit bone marrow in vitro. It might be that means of artificially increasing or lowering this resistance could shed light on the genesis of osteomyelitis.

Delayed Callus Formation from Antiseptic Treatment of Wounds.—Boerema,[43] using pigeons and hens, studied the effect of antiseptics on the healing of fractures. A 5 per cent solution of tincture of iodine or a 3 per cent solution of phenol was kept in contact with the fracture ends for three minutes after which the operative wound was sutured. A delay in callus formation was observed, when the antiseptics were used, in comparison with normal controls. This retardation in healing the author believed due to the effect of antiseptics on the specific bone building tissues, the cambium layer of the endosteum and the periosteum.

Neutralization of Poliomyelitis Virus.—Southby and McKie,[44] in an experimental investigation, showed that while the pooled serums of normal adults exhibited a definite neutralizing action for the virus of anterior poliomyelitis, this action had only from 30 to 40 per cent of the potency of convalescent serum. They also concluded that there was a definite immunologic difference between the various strains of virus.

Infection and Vaccination in Tuberculosis.—The conclusions drawn by Heimbeck [45] in his study of tuberculous infection in the commune hospital and among the population of Oslo were that allergy to tuberculosis was immunity to tuberculosis and that only a small number of persons contracted tuberculosis in childhood. Allergy indicated immunity whether produced by infection or by vaccination with BCG. Of 168 nurses vaccinated, 84 became allergic as indicated by the reaction to the Pirquet test. Of these 84 nurses, only 1 contracted tuberculosis. Of the other 84 nurses who did not become allergic through vaccination, 18 later had tuberculous infections. The author advocated repeating vaccination with BCG until allergy was produced.

Lymphatic Drainage of Joints.—Kuhns,[46] working with rabbits, found lymphatics present as abundant small vessels in the articular tissues. They were most numerous just beneath the epithelial-like layer of the synovial membrane. The lymphatic drainage of the lower extremity was through the so-called deep lymphatics to the popliteal,

43. Boerema, I.: Arch. f. klin. Chir. **176**:666, 1933.

44. Southby, R., and McKie, M.: M. J. Australia **2**:404, 1933.

45. Heimbeck, J.: Med. Klin. **29**:1731, 1933.

46. Kuhns, J. G.: Lymphatic Drainage of the Joints, Arch. Surg. **27**:345 (Aug.) 1933.

deep femoral and iliac lymph nodes. Inflammation in the synovial tissues resulted in a decreased ability on the part of the lymphatics to absorb material greater than molecular size. An apparent obliteration of the lymphatic vessels occurred when the inflammatory process was sufficiently severe or long continued.

Experimental and Clinical Observations on Tonus of Striated Muscle after Sympathectomy in Spastic Paralyses.—Kasumov [47] reported observations made on dogs in which a lumbar sympathectomy was followed by an operatively produced spastic paralysis. The sympathetic trunks were resected from the diaphragm to the first sacral segment on one side. Twenty-four days later the anterior motor roots were cut on both sides: from the fourth to the seventh lumbar and the first and second sacral. The muscle action was studied kymographically for several months. The muscles were weaker at first on the side on which sympathectomy was performed, and contractures developed much later on this side. Sympathectomy was performed on 18 children with spastic paralysis. Six showed considerable improvement, 9 slight improvement. The author believed sympathectomy was of value in weakening muscular rigidity. He advised its use in conjunction with other therapeutic measures.

47. Kasumov, G.: Sovet. khir. **4**:503, 1933.

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